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FOREWORD.

THE JOURNAL of Obstetrics and Gynæcology of the British Empire first appeared in January 1902, with the intention of being "a complete and impartial record of British work, an exponent of Obstetrical and Gynæcological practice, and a summary of contemporary thought and achievement in Obstetrics and Gynæcology throughout the world."

That the JOURNAL fulfilled, not unworthily, the objects for which it was founded cannot be denied until, like so many other activities which had no direct bearing on Victory, it ceased to exist with the advent of the Great War.

With peace, however, it was felt that the JOURNAL, which under the distinguished Editorship of Mr. Alban Doran, the late Dr. Cullingworth, Dr. T. Watts Eden and Dr. J. S. Fairbairn, had done so much for the advancement of Obstetrics and Gynæcology could not be allowed to die a natural death.

Those of the Directors still living having expressed their wish to retire from office in order that younger men should take their place, Dr. Russell Andrews, Dr. T. Watts Eden, Professor Thomas Wilson and Mr. Blair Bell were elected. The original Chairman, Sir Francis Champneys, was cordially invited to retain that office and willingly agreed.

Since the shareholders of the Company, owning the JOURNAL, first combined, solely for the purpose of advancing the Science of Obstetrics and Gynæcology and not for that of earning dividends, a new generation has appeared. It is hoped that the younger

Obstetricians and Gynæcologists, of whom there are many more now than twenty years ago, will in a similar way shoulder their share of this responsibility.

Of one thing we may be quite certain, that there is very little worth having in the world to-day which can be obtained for nothing and the JOURNAL is no exception to this rule. If it is to be kept going it must, until its circulation is sufficient, be financially supported by those who work in that field of Science with which it deals.

Every effort will be made by those who conduct the JOURNAL to ensure its success and to keep its reputation at the high level it enjoyed in the past. If sufficient support is obtained they are confident that it will again fulfil the intentions of its founders and will justify its re-birth. It is proposed, in succeeding numbers of the JOURNAL, to make a special feature of "Reviews of Current Literature."

It will be a disgrace to British Obstetrics and Gynæcology if they are not adequately represented, at home and abroad, by a Journal worthy of the Nation and the Speciality. It is up to the younger school to do their utmost to ensure that such an object is attained.

COMYNS BERKELEY.
EARDLEY HOLLAND.

The Toxæmias of Pregnancy, with Special Reference to the Value of Certain Renal Function Tests in Diagnosis.

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I. Introduction.

The significance of certain abnormal constituents in the urine of pregnant women is often doubtful, and this applies more particularly to the occurrence of albumen. The work which the writer has carried out since 1912 on this particular subject is embodied in the present paper. It represents one portion of a somewhat elaborate enquiry into the value of certain tests for assessing the functional activity of the pancreas and kidneys. The work on the pancreas has already been published,[1] as also the observations made on nephritis.[2] The latter work was carried out in collaboration with Dr. Langdon Brown and Dr. Trevan, and the results recorded in various papers published in 1915 and 1916. With this opportunity of acquiring considerable experience of renal function tests rendered possible by an outbreak of acute nephritis in France in 1915, it has been possible to apply this knowledge in the present enquiry. Practically every case of albuminuria admitted to the maternity wards of St. Bartholomew's Hospital has been investigated, and this has only been possible through the help and ready co-operation of the visiting staff of the Maternity Department. To prove the value of the tests as an aid in differential diagnosis was the primary object of this work. Having established the means whereby a differentiation can be made between the true toxæmias of pregnancy and nephritis occurring in pregnancy, the next stage is to elucidate the possible cause or causes of the former condition. The success of the tests depends upon the early recognition of a toxæmia or nephritis in pregnancy since many of them are "fleeting" in character, and should therefore be carried out as soon as possible. The results so obtained will thus serve as an aid to diagnosis and treatment and give satisfaction to the obstetrician and pathologist, and benefit to the patient.

II. Scheme of Procedure.

The essential link in the chain of investigation is the possession of an ante-natal department. Here the cases are seen and the urine tested. Every pregnant woman who is found to be passing albumen or shows any signs of toxæmia or nephritis can then be investigated on the following lines. The scheme of investigation which has been followed consists of :—

1. An examination of a catheter specimen of urine for (*a*) the amount of albumen and globulin present, and the ratio of one to the other; (*b*) the presence of casts; (*c*) the diastase content. This examination can be carried out in an hour.

2. The collection of blood from an arm vein, and the estimation of the urea, non-protein nitrogen, sugar, etc.

3. Cerebro-spinal fluid when available for general examination and estimation of urea and sugar content, also reaction.

4. Complete urinary analyses on a fixed dietary for estimation of normal and abnormal constituents, especially chlorides, total nitrogen, urea, ammonia, and amino acids.

5. The urea concentration test of MacLean.[3]

The order in which these tests are carried out and the actual number performed depends largely upon circumstances, and when there is great urgency, only the urine and blood analysis viz., 1 and 2 in the scheme above are possible. As a general rule when a patient is admitted with albuminuria it is possible to carry out all the necessary tests in the course of three days. In cases of suspected toxæmia or when complications of a similar nature have occurred in a previous pregnancy it has been the custom to make an estimation of the diastase content of the urine and to watch the progress of the case by fortnightly examinations from the fourth month onwards. The same applies to nephritis in pregnancy with an occasional analysis of the blood as well. The full scheme of investigation is of course the ideal, but rarely possible of attainment at the present day.

III.—Methods of Analysis.[1]

(*a*) *The diastase content of the urine.*

The presence of a ferment capable of digesting starch solutions when added to urine has been known for a very long time. The subject received new interest when in 1909 Wohlgemuth[4] pub-

1. The necessary apparatus, etc., for carrying out the methods described in this paper may be obtained from Messrs. Gallenkamp and Co. Ltd., 19–21, Sun Street, Finsbury Square, E.C.1.

lished his method of estimating the amount of diastase in the urine. He showed that in pancreatic disease the diastase content of the urine was markedly increased. Since these observations were recorded a number of workers have all obtained confirmatory evidence, but the best and most complete work is undoubtedly that of Corbett[5] in this country. He showed that there is normally a certain amount of diastase in the blood and that the same quantity is excreted by the kidneys. If there is an increase of diastase in the blood then there is a corresponding increase in the amount of diastase in the urine provided that the kidneys are functionally unimpaired. The slightest damage to the renal epithelium leads either to a great diminution of diastase in the urine, or an increase depending upon the permeability of the kidney. Geyelin[8] came to similar conclusions as regards the influence of the kidneys in the removal of diastase from the blood. With regard to pancreatic diseases it is of interest to note that Wohlgemuth and Noguchi found an increase of diastase in both blood and urine when injury to the pancreas had occurred. The results of Corbett[5] are also striking, and there seems to be no doubt that a high diastase value of the urine is in favour of pancreatic disease whereas a normal or low value points to a normal pancreas. Some writers, however, have suggested that these high values are only obtained in the acute stages of the disease. These observations represented the general trend of opinion when I first commenced my work upon the subject. The analysis of my results will be given later, and compared with the various other tests that have been applied. In carrying out the estimations I have followed the technique devised by Wohlgemuth in certain particulars, and the method of procedure is as follows.[7]

A twenty-four hours hourly collection of the urine is made into clean stoppered glass bottles, and the estimation is carried out as rapidly as possible after the full amount has been collected. The urine should be as free as possible from contamination, and when a twenty-four hourly specimen is unobtainable I generally advise a six-hourly collection, or better still a twelve-hourly collection. Apart from the fact that there may be a slight rise in the diastase content of the urine preceding a meal followed by a fall immediately afterwards and lasting for from three to four hours, the rise is so slight that it is almost negligible except when attempting to obtain normal standards of diastase excretion. For practical purposes it does not matter whether a fresh specimen, or a twenty-four hours hourly sample of urine is used. To preserve the urine when facilities for carrying out the test are not immediately available, toluol is added. This will not affect the diastase, and in fact specimens may be kept for months or even years without showing

any alteration in their diastase content. All other forms of preservative must be avoided since I have found that in most cases they lead to immediate destruction of the ferment.

For the actual test only 2—3 cc. of urine are required. The apparatus and chemical reagents required are :—

(1) Ten clean dry test tubes made of good glass of equal bore, and of uniform thickness.

(2) Standard 10 cc. burettes, Ostwald pipettes of 1 cc. and 2 cc. capacity, and 1 cc. pipettes graduated in $^1/_{100}$ths of a degree.

(3) Pure distilled water.

(4) A carefully prepared solution of starch made by dissolving 2 grams of pure soluble starch in 100 cc. of pure 10 per cent. sodium chloride. This acts as a stock solution and the standard starch solution is made up fresh as required. 5 cc. of this stock solution are placed in a 100 cc. measuring flask and diluted up to the mark with pure distilled water. This solution now contains 0.1 gram per cent. of soluble starch in a 0.5 per cent. solution of sodium chloride, and is the solution used in all the diastase estimations recorded in this paper.

(5) A $^1/_{50}$th normal solution of iodine. This has to be made up fresh as required since it does not keep well particularly in the summer months. The iodine solution is stored in the dark in $^1/_{10}$th normal strength, and from this a fresh $^1/_{50}$th normal solution is made by diluting 2 cc. of the iodine solution up to 10 cc. with distilled water. A specially prepared dropping pipette is always used with this solution to ensure that the same number of drops of dilute iodine are added to each tube when carrying out the estimation.

(6) A reliable water bath which is maintained at a temperature of 39° C. by means of a thermo regulator.

(7) A wire cage to hold the test tubes in place when immersed in the bath.

The tests are carried out as follows :—The 10 test tubes are placed in a stand and numbered in sequence. 1 cc. of the urine to be tested is added to tube No. 1 by means of a pipette, and tube No. 2 contains .5 cc., and so on according to the table below. Each tube is then made up to a volume of 1 cc. with distilled water. We have now a series of 10 test tubes containing various decreasing quantities of urine, but each of equal volume—1 cc. It has been found that by careful manipulation and using a good pipette that this method of dilution gives rise to only a slight error, at least insufficient to affect the estimation.

We now have the following series of dilutions:—

(1) – 1 cc. of urine
(2) – 0.5 cc. „
(3) – 0.2 cc. „
(4) – 0.1 cc. „ (1 cc. urine diluted with 9 cc. water)
(5) – 0.08 cc. „
(6) – 0.06 cc. „
(7) – 0.04 cc. „
(8) – 0.02 cc. „
(9) – 0.01 cc. „ (1 cc. of 1 in 10 diluted with 9 cc. water)
(10) – 0.008 cc. „

All these tubes are now inserted into the wire cage and placed in the water bath for 15 to 30 minutes. This serves to bring the temperature of the mixtures up to the required level, and further activates the ferment present in the urine. The diluted starch solution is now run into each tube, 2 cc. being used, and after mixing the tube is replaced in the wire cage. The wire cage is placed in the water bath and allowed to remain there for half an hour, after which time the cage is withdrawn, placed in running water to cool the tubes, and to arrest any further ferment action. The 10 tubes are replaced in the test tube stand in their original order. By means of the fine dropping pipette two drops of the freshly prepared iodine solution are added to each tube and the mixture shaken.

If the urine is normal tubes 1, 2 and 3 show a golden yellow colour, indicating that the 2 cc. of starch solution added has been completely digested by the diastase present in the urine. Whilst tube 4 will have a reddish colour with no tinge of blue, tube 5 a violet tinge, and all the remaining tubes will be deep blue. In such a series tube 4 will give the reading required since it is the tube in which the starch has been digested as far as the dextrin stage. This red-coloured tube is taken as the limit tube when the above dilutions are used. After considerable experience with this method I prefer to adopt this reading rather than the somewhat indefinite mauve tint.

The calculation of the amount of diastase in the urine is now a simple matter, the results being expressed in terms of units of diastase. Thus tube 4 gives a red colouration and shows that 0.1 cc. of the urine has digested 2 cc. of a .1 per cent. solution of starch in half an hour at a temperature of 39° C.
Therefore 1 cc. of urine will digest

0.1 : 2 cc. starch : : 1 cc. : x.

This gives a diastase content of 20 units, or, in other words,

1 cc. of the urine is capable of digesting 20 cc. of an 0.1 per cent. solution of starch in half an hour, or expressed numerally :

$$d\,\frac{39^{\circ}}{30} = 20 \text{ or } d = 20 \text{ units.}$$

In dealing with urines from cases of toxæmias of pregnancy the above method possesses many advantages since the 10 tubes give a wide range, and the differences are generally so large that minor errors of dilution, changes in volume of the urine, saline constituents, reaction, and presence of abnormal constituents have very little influence on the result. Thus we see how important it is to adopt a technique with freedom from any external sources of error, and any attempt to depart from this procedure either on the lines of simplification or amplification invariably meets with failure. After an extensive trial with this test on many hundreds of specimens of urine it has been possible to fix a standard for normal healthy individuals. The normal average value has been found to be 20 units, the maximum being 33.3 and the minimum 10 units—a sufficiently limited range from which to determine whether a given urine is normal or abnormal.

(*b*) *Analysis of the blood.*

For a complete analysis of the blood the methods devised by Folin and Wu[8] have been followed with certain modifications. The blood is obtained by venepuncture of an arm vein, the sample being taken at least three hours after a meal. The blood is allowed to flow into a small measuring cylinder containing a small amount of powdered potassium oxalate to prevent clotting. The potassium oxalate should not exceed 20 milligrams, and this acts best when distributed over the sides of the cylinder. For the analysis either 7 cc. or 12 cc. of blood are removed, the latter volume being obtained for preference. Immediately the amount required has been collected the cylinder is thoroughly shaken to prevent clotting and 5 cc. or 10 cc. of the oxalated blood is removed by means of a standard pipette and placed in a clean Erlenmeyer flask. The blood is now diluted with seven times its volume of distilled water and thoroughly shaken until complete laking has been obtained. To this mixture is added first a 10 per cent. solution of sodium tungstate and then two-thirds normal sulphuric acid in equal proportions. Thus if 10 cc. of blood are used 70 cc. of distilled water is added, then 10 cc. of 10 per cent. sodium tungstate, and 10 cc. of two-thirds normal sulphuric acid. This makes a total volume of 100 cc. If only 5 cc. of oxalated blood is used then just half the quantity of the other reagents are required, and the resulting volume is 50 cc.

This mixture at first assumes a bright red colour, but a preci-

pitate soon appears which rapidly converts the mixture to a dark brown colour. The whole is now thoroughly shaken until it becomes viscous and produces a metallic ring when shaken, similar to that produced by shaking mercury in a glass vessel. The blood mixture may now be filtered, and the filtrate is remarkable for its clarity and brilliant watery appearance. This filtrate is almost neutral in reaction or at the most faintly acid provided pure reagents are used. It contains no trace of proteins, but all the uric acid, creatinin, urea, and sugar are present in this filtrate. This method of preparing a protein-free filtrate from blood is superior to any other method so far devised, and provided due care is taken is always successful.

The urea content of the filtrate is estimated by means of the urease method. Five cc. of the clear filtrate are digested with an alcoholic extract of soya beans, and the resulting ammonium carbonate formed from the urea by the ferment urease is distilled in the presence of borax. The ammonia which distils over is collected in standard acid and estimated by means of Nessler's reagent. The colour obtained is compared in the colorimeter against a similar test carried out on a standard solution of urea made up in such a strength as to yield a colour comparable with that of a normal blood urea content. This estimation can be carried out in a short time, and judging by a number of control experiments gives remarkably constant results. My colleague, Mr. H. E. Archer, Demonstrator of Pathology, is at present engaged on the method of estimation of urea in the blood, and his results will be published shortly.

The sugar content of the blood is estimated on the filtrate according to the method described by the writer and Dr. C. D. Gallagher.[9]

(*c*) *The cerebro-spinal fluid.*

The same constituents, viz., urea and sugar, are estimated whenever lumbar puncture is performed for diagnostic purposes. The results of the blood analysis are, however, much more conclusive, and the results of an analysis of the cerebro-spinal fluid are used simply to confirm the figures obtained for the blood.

(*d*) *The urinary proteins.*

The presence of globulin in the urine is of significance especially if the amount present is estimated and the ratio of albumen to globulin determined.[10] The method of estimation of the total protein in the urine, and the globulin content consists in refractometer readings, and also using the nephelometer, and estimating the degree of turbidity. For this purpose a small amount of urine

is required, and the estimation can usually be carried out on a catheter specimen.

The following tests for globulin in the urine may also be applied :—

(1) To about 10 cc. of the urine in a test tube add three to six drops of dilute acetic acid (33 per cent. strength). The presence of an excess of globulin is indicated by the immediate appearance of an opalescence or precipitate. If the precipitate appears after some time this is not due to globulin but to mucin. Care should be taken to use dilute acetic acid, and not to add more than six drops as otherwise the globulin is re-dissolved.

(2) The distilled water test of Roberts. This test consists in adding the urine drop by drop to a tall cylinder containing distilled water. In the presence of globulin a white ring appears as the drop falls through the distilled water, resembling smoke rings. This test does not yield positive results unless there is a large amount of globulin present, and is not so delicate as the precipitation test produced by the addition of acetic acid in the cold.

(*e*) *The urea concentration test.*

This useful and at the same time simple test, devised by MacLean,[3] has been given an extensive trial, and the results have fully justified its use in every case in which the question of renal function arises. It can be carried out without any inconvenience to the patient, and does not require elaborate apparatus. The details of the test are as follows :—

The patient is instructed to empty the bladder in the morning, and on a fasting stomach is given the following mixture by the mouth : 15 grammes of urea dissolved in 100 cc. of water, and flavoured with a little tinctura aurantii. Exactly one hour after the dose has been consumed the bladder is emptied and the specimen passed is placed in a bottle and labelled specimen No. 1. Then again at the end of the second hour the bladder is emptied and this specimen labelled No. 2. The urea content of each of these specimens is estimated by the ordinary hypobromite method, which is sufficiently accurate for the purpose. The results are recorded in percentage of urea passed in each specimen. It is often advisable to collect the urine passed three hours after the urea solution has been consumed.

IV.—The Results Obtained.

The following results have been obtained from an investigation of a number of cases admitted to the maternity wards. In all, twelve undoubted cases of toxæmia of pregnancy have been examined, and twenty cases of nephritis in pregnancy. These

cases have all been in hospital during the time the full scheme of procedure outlined above was in operation, but a large number of cases investigated from 1912 to 1914 have been omitted since the details were not complete. In addition a large number of non-pregnant women, normal pregnant women, and pregnant women presenting various complications of pregnancy, have been investigated, more especially for purposes of control observations.

(*a*) *The results of analysis of the blood.*

In toxæmias of pregnancy the results of an analysis of the blood show no striking deviations from those found in normal pregnant women. The blood urea content is usually within the normal limits of 0.02 to 0.05 gram. per cent. The same applies to the sugar in the blood which is nearly always normal, viz. 0.08 to 0.110 gram per cent. These results are of particular interest, especially when considered in relation to the high values found for diastase in the urine. The constant association of a high diastase value with hyperglycæmia and glycosuria in diseases of the pancreas has been pointed out by the writer.[1] In the toxæmias of pregnancy all attempts to incriminate the pancreas have so far failed in that the functional tests gave negative results. A disturbance of function of almost all the ductless glands is reflected in the blood sugar content, and a consequent disturbance of carbohydrate metabolism. The fact that the blood sugar content is normal in this condition would negative the view that the toxæmias of pregnancy are associated with one or more of the endocrine glands.

The blood sugar tests and sugar tolerance tests are the only real means we have at present of testing the functional activity of the ductless glands. If then the toxæmias of pregnancy are due to a loss of balance between these glands then the mechanism must be of such a delicate nature that the disturbance is not reflected upon carbohydrate metabolism. In all my investigations I have not found a case of eclampsia or toxic vomiting showing hyperglycæmia or glycosuria; neither have I seen any case of glycosuria in pregnancy develop a toxæmia. The existence of such cases is extremely problematical. That the toxæmias of pregnancy are due to a ductless gland deficiency has been frequently suggested, but upon very doubtful evidence, and my results are in direct opposition to any such hypothesis.

The same remarks apply to all the other constituents of the blood which have been estimated.

(*b*) *The relation of albumin to globulin in the urine from cases of toxæmia of pregnancy.*

The figures given in the tables appended show the total protein

content of the urine in this condition. The protein in the blood serum may be separated into albumin and globulin, and these same two proteins appear in the urine under certain conditions. The actual amounts of each protein present has been determined by various methods, and it has been found that the ratio of albumin to globulin is of distinct diagnostic value. This conclusion is emphasized by reference to the following table :—

TABLE SHOWING ALBUMIN TO GLOBULIN RATIO IN VARIOUS RENAL CONDITIONS.

	Albumin.	Globulin.	Diastase output.
Nephritis	6	1	low
Functional albuminuria ...	2	1	normal
Leaky kidney	1	2	normal
Toxic albuminuria ... ... (Eclampsia, etc.)	2	1	high

The figures given represent the average values found in a large number of cases of the four types investigated. It will be seen that the toxic albuminuria group can be readily distinguished from the true nephritis by means of this ratio. There is a relatively larger amount of globulin present in the urine of toxæmias of pregnancy, and this is of such constant occurrence as to warrant attention. In addition to this constant appearance of globulin we have generally a larger amount of total protein present in the urine in toxæmias of pregnancy. Globulin whenever it occurs in the urine produces a very heavy precipitate, so much so that the urine is often said to "set almost solid" on boiling. So flocculent may the precipitate appear that we are led to the conclusion that very large amounts of protein are present in the urine. On estimating the actual amount of protein present by gravimetric methods we find that the figures are much lower than was expected from the bulkiness of the precipitate. For clinical purposes the ratio of albumin to globulin is not easy to obtain as the estimation is tedious and time consuming. There are, however, two tests which can be applied without the use of elaborate apparatus and a well-equipped laboratory, and these are the acetic acid in the cold test, and the distilled water test. These two tests have been described above, and if both yield positive results the conclusion is that globulin is present in the urine in relatively large amounts. The occurrence of such a globulinuria in the toxæmias of pregnancy is of great interest, and warrants further enquiry. The globulinuria of the functional albuminuria type, I am of opinion, is largely vascular in origin. There is a "blushing" of the kidney and a passage of globulin through the renal epithelium resembling in

character that which occurs in a passive exudate.[10] In eclampsia the most common change which we see in the kidneys consists of a distinct swelling of the walls of the capillaries of the glomeruli. Further, the presence of hæmoglobin casts is frequently met with. The toxin of eclampsia, in my opinion, exerts its main action on the blood and blood vessels. In the case of the kidneys this action is most obvious in the glomeruli where the capillary tufts are the first to be involved. There is thus an acute glomerulitis or, using the nomenclature of Volhard and Fahr,[11] a nephrosis; and this accounts for the presence of globulin in the urine in relatively large amounts in eclampsia, as also the increased diastase output described in this paper. The same action of the toxin on the cerebral vessels may explain the occurrence of eclamptic fits. Here again we get acute cerebral œdema, and the cessation of the fits after lumbar puncture is thus explained.

(*c*) *Diastase content of the urine.*

In normal pregnant women the diastase content of the urine is remarkably constant and does not differ from that found in non-pregnant women or healthy males. The results expressed in units give average values ranging from 10 to 33.3 units.

The toxæmias of pregnancy on the other hand show most striking differences as regards the diastase content of the urine. After an investigation of the normal and pathological variations in the diastase content of the urine in which many hundreds of estimations have been made, this fact has been strongly emphasised.[7] Apart from diseases of the pancreas this is the only condition in which such high values have been found, either under normal or pathological conditions. All attempts to incriminate the pancreas as being involved in the toxæmias of pregnancy, either directly or indirectly, have so far failed. My "tripod" of tests[1] have been tried on a number of cases, but only the diastase test has yielded positive indications in that the diastase content of the urine was abnormally high. There was no glycosuria in any case, no hyperglycæmia, and Loewi's adrenalin mydriasis test was constantly negative. These high values for diastase were found both in the true toxic vomiting of pregnancy and also in eclampsia. By carefully watching the patients in the wards it was found that the diastase estimation provided the earliest sign of the onset of toxæmia. The diastase content suddenly increased to be followed a few days later by signs of toxæmia. Again it was found that the diastase content remained abnormally high after all other signs and symptoms of toxæmia had disappeared. These observations are of more than passing interest and lead one to speculate upon the possible cause of toxæmia and the effect of the toxin in increas-

ing renal permeability. The blood diastase content in eclampsia is quite different to that in pancreatic disease in that there is no marked increase in the blood diastase in the former condition. The toxin acts on the capillary tufts of the glomeruli, and causes a rapid elimination of the diastase in the urine. This is in direct contrast to that met with in the nephritis in pregnancy in which the diastase content of the blood is increased whilst that of the urine is diminished, depending on the actual renal permeability. The greater bulk of the patients in whom albuminuria is detected during pregnancy belong to this class, and are generally suffering from chronic parenchymatous nephritis ranging from a mild to a more severe type. It is in this type that the diastase estimation in the urine is of such value, especially when combined with the other well recognized renal function tests. Usually it is found that the diastase content is below 10 units, the actual figure depending very largely on the extent of renal damage. Thus a moderately severe form of nephritis may show a diastase content of 5 units, whereas the more severely damaged kidneys give values of 3 units, or even less. This estimation, therefore, gives one a very good idea of the extent of renal damage, and in addition has been used for prognosis.

Again the test may be used for the early detection of renal insufficiency in pregnancy, and has been so used by the writer. A patient who was diagnosed as eclamptic in a previous pregnancy showed no albuminuria and a diastase content of 20 units in the fourth month of the succeeding pregnancy. A month afterwards the diastase content fell to 5 units, and trouble was expected. The urine was examined at fortnightly intervals, and in the next specimen albumen appeared together with casts, and 5 units of diastase. On this result the patient was put to bed, given a low nitrogen diet, and the urinary output increased. The albumen has increased, but the casts have disappeared, and the diastase content is still 5 units. There is no œdema; and the patient is progressing favourably. There seems little doubt that the symptoms observed in the previous pregnancy were due to nephritis in pregnancy, and not to eclampsia. Many cases regarded as eclampsia have been proved to be nephritis in pregnancy on these tests, and treated accordingly.

In striking contrast to the variations in the diastase content of the urine in these conditions we have a number of results on the ordinary so-called neurotic vomiting in pregnancy. In this exceedingly common complication of pregnancy the diastase content has been found to be normal. The vomiting of course leads to the appearance of acetone bodies in the urine, and with it a high ammonia co-efficient. This ammonia co-efficient I have found much higher in this condition than in the true toxæmias of pregnancy, and consequently this estimation does not give results of

any value either for diagnosis or prognosis. The pregnant woman is always in a state of unstable equilibrium as regards carbohydrate metabolism, and the excessive vomiting at once leads to the appearance of acetone bodies in the urine. She requires carbohydrates, and if these are withheld either by dietary restrictions or to excessive vomiting then fats begin to be improperly and abnormally metabolised. In such a condition more harm is done by giving fats than by withdrawing them from the diet. The favourable results obtained by the administration of a high protein and carbohydrate diet in this condition will be recorded in another paper.

V.—Table of Cases.

Case 1. A. C. Toxæmia of pregnancy—pre-eclamptic stage. Urine.—Albumen, 6.5 grams per cent.; globulin present; ratio of albumen to globulin, 1:1. Diastase.—50 units. Blood.—Urea=0.06 gram per cent. Urea concentration test.—1st hour, urea=1.1 per cent; 2nd hour, 1.0 per cent.

Case 2. I. S. Eclampsia. Urine.—Albumen present. Diastase.—200 units. Blood—Maternal—Urea=0.02 gram per cent.; fœtal, urea=0.02 gram per cent. Cerebro-spinal fluid—Urea=0.02 gram per cent. Wassermann reaction—negative. Cæsarean section.

Case 3. E. G. Toxic vomiting. Urine.—Diastase=100 units. Aceto-acetic acid present in quantity. After a high protein diet: Urine.—Diastase=25 units. Aceto-acetic acid absent. Cured in a week.

Case 4. K. B. Toxic vomiting. Urine.—Albumen present in small amount. Aceto-acetic acid present. Ammonia coefficient=3. Diastase=50 units. Induced labour. Urine, five days after.—Diastase=50 units. Albumen absent. Aceto-acetic acid absent. Urine seven days after—Diastase=20 units. Albumen absent. Aceto-acetic acid absent.

Case 5. A. B. Toxic vomiting. Urine.—Albumen absent. Aceto-acetic acid present. Ammonia coefficient, 15. Diastase=100 units.

Case 6. J. A. Nephritis in pregnancy. Urine.—Albumen, 0.25 per cent. Globulin absent. Diastase=2.5 units. Blood.—Urea=0.27 gram per cent. Urea concentration test.—1st hour, 1.1 per cent.; 2nd hour, 1.1 per cent. Remarks.—Blood pressure, 260 mm.; slight œdema; albuminuric retinitis; spontaneous miscarriage 22nd week.

Case 7. G. O. Nephritis in pregnancy. Urine.—Albumen present. Diastase=3.3 units. Blood.—Urea=0.03 gram per cent. Sugar=0.085 gram per cent. Urea concentration test.—1st hour, urea=1.0 per cent.; 2nd hour, 1.1 per cent. After delivery: Urine.—Albumen present; fatty and hyaline casts present. Diastase=20 units. Cerebro-spinal fluid.—Urea=0.045 per cent. Ascitic fluid.—Urea=0.02 per cent. Recovered.

Case 8. E. G. Nephritis in pregnancy. Urine.—Albumen present; casts present. Diastase = 5 units. Blood.—Urea=0.19 gram per cent. Cerebro-spinal fluid.—Urea=0.08 gram per cent. Remarks: Coma and

fits; Cæsarean section performed; patient died. Autopsy: small white kidneys and Pontine hæmorrhage found.

Case 9. G. D. Nephritis in twin pregnancy. Urine.—Albumen, 0.3 gram per cent. Diastase=5 units. Blood.—Urea=0.039 gram per cent. Urea concentration test.—1st hour, urea=1.3 per cent.; 2nd hour, 0.6 per cent. Nine days later: Urine.—Albumen present. Diastase=3.3 units. Blood.—Urea=0.48 gram per cent. Induced labour on result of this report. One child died, the other recovered. After delivery: Urine.—Albumen present. Diastase=5 units. Urea concentration test.—1st hour, urea, 1.1 per cent.; 2nd hour, 1.9 per cent.

Case 10. F. W. Nephritis in pregnancy. Urine.—Albumen, 0.2 per cent. Diastase=10 units. Blood.—Urea=0.018 gram per cent.; sugar=0.100 gram per cent. A fortnight later patient developed signs of infection. Blood.—Urea=0.043 gram per cent. No fits, and no signs of uræmia. Patient died. Post mortem.—Large white kidneys found.

Case 11. J. C., 23. Nephritis in pregnancy. Urine.—Albumen present. Diastase=3.3 units. Blood.—Urea=0.028 gram per cent.; one month later, 0.052 gram per cent. Urea concentration test.—1st hour, urea=1.4 per cent.; 2nd hour, 1.0 per cent. Urea concentration test one month later.—1st hour, urea=0.9 per cent.; 2nd hour, 1.8 per cent. Remarks: Recent retinitis; B.P. 178; Wassermann reaction, negative; lesion progressive, and albuminuria still present two months after abortion.

Case 12. S. H. Nephritis in pregnancy. Urine.—Albumen present. Diastase=6.6 units; casts present. Blood.—Urea=0.049 gram per cent. Urea concentration test.—1st hour, urea=0.9 gram per cent.; 2nd hour, 1.2 grams per cent. Remarks: Retinitis; no œdema; mid-term pregnancy terminated by still birth; condition did not clear up and lesion progressive as evidenced by retinitis and albuminuria one month later.

Case 13. S. Mitral regurgitation. Urine.—Albumen absent. Diastase=33.3 units. Blood.—Urea=0.03 gram per cent. Induced labour, and recovery.

Case 14. L. F Neurotic vomiting of pregnancy. Urine.—Albumen absent. Diastase=10 units. Aceto-acetic acid present. Recovered on dieting with high protein diet.

Case 15. McD. Puerperal Insanity, epilepsy. Urine.—Albumen present; globulin present. Total protein=0.925 per cent.; diastase 10 units. Blood.—Urea=0.014 gram per cent. Cerebro-spinal fluid.—Urea=0.05 gram per cent. Remarks: Fits; Cæsarean section; transferred to asylum.

Case 16. F. H. Pyelitis in pregnancy. Urine.—Albumen absent. Diastase=33.3 units. Blood.—Urea=0.02 gram per cent. Urea concentration test.—1st hour, 1.0 gram per cent.; 2nd hour, 2.2 grams per cent.

Case 17. B. Chronic interstitial nephritis. Urine.—Albumen, traces. Diastase=3.3 units. Blood.—Urea=0.1 gram per cent. Urea concentration test.—1st hour, urea=0.9 gram per cent.; 2nd hour, 0.8 gram per cent. Remarks: B.P., 115 mm.; no eye changes.

TOXÆMIAS OF PREGNANCY.

	Urine, Albumen.	Globulin.	Diastase in Units.	Blood, Urea.	Concentration. 1st hr. Urea	2nd. Urea
	%			%	%	%
1. A.C.: Eclampsia	6·5	++	50	0·06	1·1	1·0
2. J.S.: Eclampsia	+	++	200	0·02	—	—
3. Toxic vomiting	+	+	100	—	—	—
2 weeks later	0	0	25	—	—	—
(after high protein diet.)						
4. K.B.: Toxic vomiting ...	+	+	50	—	—	—
Induced labour	0	0	50	—	—	—
5 days after	0	0	—	—	—	—
7 days after	0	0	20	—	—	—
5. A.B.: Hyperemesis gravidam	0	0	100	0·02	—	—
6. A.D.: Eclampsia	0·225	+	200	0·02	—	—
7. N.D. (Hepatic)	+	+	200	—	—	—
8. G.B.: Eclampsia	0·55	+	100	—	—	—
9. E.S.: Eclampsia	+	+	200	0·02	—	—
10. M.L.: Eclampsia	0·15	+	200	—	—	—

NEPHRITIS IN PREGNANCY.

	Urine, Albumen.	Globulin.	Diastase in Units.	Blood, Urea.	Concentration. 1st hr. Urea	2nd. Urea
	%			%	%	%
1. J.A.	+0·25	0	2·5	0·27	1·1	1·1
2. G.O.	+	0	3·3	0·03	1·0	1·1
After delivery	+	0	20	0·04	1·0	1·8
3. E.G.	+	0	5	0·19	—	—
4. G.D.	+0·3	0	5	0·039	1·3	0·6
9 days later	+	+	3·3	0·48	—	—
After delivery	+0·02	0	5	—	1·1	1·9
5. F.W.	+0·2	0	10	0·018	—	—
2 weeks later	+	—	—	0·043	—	—
6. A.J.	0·65	0	5	0·06	—	—
7. C.S.	0·05	0	5	—	—	—
8. E.C.	0·1	0	4·0	—	—	—
9. J.C.	0·225	0	3·3	0·028	1·4	1·0
1 month later	—	—	—	0·052	0·9	1·8
10. S.H.	+	0	6·6	0·049	0·9	1·2

PREGNANCY: OTHER CONDITIONS.

	Urine, Albumen.	Diastase.	Blood, Urea.
	%	in Units	%
1. Neurotic vomiting: L.F.	0	10	—
2. Mitral regurgitation: S.	0	33·3	0·03
3. Ante-partum hæmorrhage: subacute	0·2	10	0·018
nephritis ... ... later ...	—	—	0·043
4. Epilepsy: puerperal insanity	0·92	10	0·014
5. Mitral regurgitation	0	10	0·072
6. Pyelitis	0	33·3	0·02
7. Chronic interstitial nephritis	traces	3·3	0·1

Summary and Conclusions.

The object of the work recorded above was primarily to ascertain the value of certain renal function tests in their application to the albuminurias of pregnancy. Certain well-known tests have been selected and applied as far as possible to every case. This selection has been made after an extensive trial of the various renal function tests, and from information gained as to their individual or collective worth in diagnosis. The four tests described in this paper appear to yield data of the first importance not only for assessing the extent of renal damage in any given case, but also in the differentiation of the various types of albuminuria met with in pregnancy. The urinary diastase test would appear to yield the most conclusive evidence of renal insufficiency, and at the same time appears to be the most delicate. The consistent low values found in nephritis in pregnancy are strikingly illustrated by reference to the table in the text. The number of units of diastase also bears some relation to the actual extent of renal damage at the time of examination, and consequently this test may be used for prognosis. In these respects the estimations of urinary diastase recorded above agree very well with the author's previously published conclusions on acute nephritis.[4] The diastase output was thus used both for diagnostic and prognostic purposes in 1915, and was found to yield as much if not more information than any other single test for renal function. Apart from its value in nephritis either of the acute, chronic parenchymatous, and chronic interstitial type, the test is found to give valuable evidence of the early onset of toxæmias of pregnancy. In striking contrast to nephritis we find excessively high values in all cases of toxæmias of pregnancy. This high value has been found in cases of toxæmia before any of the usual signs or symptoms have developed, showing that the toxin or toxins produced, exerts a profound and early effect on the mechanism concerned with the production and elimination of diastase in the body. Not only is the increased diastase output indicative of a developing toxæmia, but the rise is found to persist for some time after all the other signs and symptoms have vanished. These characteristic features of the diastase output were fortunately recognized quite early in the investigations which form the subject of this paper, and as a result it has been the custom to do a diastase estimation in every suspected case of toxæmia, no matter how slight the clinical evidence may be. The figures given in the table of toxæmias of pregnancy are sufficiently striking and do not require further description here. The investigation of any case of albuminuria in pregnancy should therefore commence with an analysis of a fresh specimen of urine for albumen, globulin,

casts, and the diastase content. In a case of suspected toxæmia this should be sufficient, since all the other tests yield results, which strictly speaking, are negative in their indications. The only other test which appears to be of diagnostic import is the estimation of the ratio of albumen to globulin, though this is not always so reliable, and suffers from the disadvantage of being time consuming and complicated.

The cases of nephritis in pregnancy, on the other hand, present so many and varied aspects that no one test has been found to be absolute in its diagnostic indications. It is here that we require to apply all four tests before coming to any conclusion as to the efficiency of the kidneys. The observations recorded in the paper, and illustrated by reference to the table of cases of nephritis in pregnancy, prove conclusively that no one test is capable of yielding all the information we require. The presence of albumen and casts, together with a subnormal diastase output, is provided by the first analysis in the scheme of procedure adopted. The analysis of the blood is, however, of particular importance both for diagnosis and prognosis, and this refers more particularly to the urea content. We know that normally the blood contains from 0.02 to 0.05 gram per cent. of urea, and that the same amount is usually present in the cerebro-spinal fluid. When instead of a normal content we find 0.1 per cent. we know that there is some degree of urea retention. The urea content of the blood may rise above this level up to even 0.8 per cent., but at this figure the issue is usually fatal. As a general rule we place the maximum urea content of the blood compatible with life, at or about 0.3 per cent. One case is recorded in this paper in which the urea in the blood was 0.48 per cent., and this patient recovered, whereas a patient with a blood urea content of 0.19 per cent. died of uræmia.

The estimation of the urea in the blood is of value as indicating whether there is urea retention, and therefore diminished renal function, and also gives a good basis for prognosis in some cases of nephritis in pregnancy. This is well illustrated by reference to Case 9 in this series in which the retention of urea in the blood was the only indication of a severe and progressive nephritis. As a result of this analysis labour was induced, and the life of the mother saved. In spite of this marked urea retention this patient showed no obvious signs of uræmia, but was undoubtedly in the danger zone sufficient to warrant immediate termination of the pregnancy. The records of a large number of cases of both acute and chronic nephritis investigated at St. Bartholomew's Hospital show that the urea content of the blood does not give any clue as to the imminence of uræmia. The characteristic syndrome of uræmia may develop quite insidiously, and especially is this so with the chronic

type of case. In nephritis in pregnancy, on the other hand, many cases with severe renal damage and definite urea retention appear to be always on the brink of uræmia, and it requires very little additional strain to bring on uræmic convulsions and coma. The estimation of urea in the blood is at the best of secondary importance, and of very little value by itself either for diagnosis or prognosis. The excellent and simple test devised by MacLean and fully described in this paper has proved to be of distinct practical value in the diagnosis of nephritis in pregnancy. After the dose of urea by the mouth the normal urea concentration in the urine is either 2 per cent. or more. The degree of renal insufficiency is gauged by the estimation of the urea concentration in the urine one hour and two hours after the dose has been given. A urea percentage of 1.5 indicates that there is moderate damage to the kidneys, whereas a low concentration of 1 per cent. or under indicates that there is severe damage. Referring to the list of cases in which this test has been applied, on several occasions we find that the concentration of urea is in every case below 1.5 per cent. This inability of the kidney to concentrate urea presupposes a retention of urea in the blood, but this is not found to be the case in my series. In the pregnant woman we are dealing with a combination of factors apart from the question of renal function. The test does, however, indicate that at the time of application there is severe damage to the kidneys in almost every case of nephritis in pregnancy. They, however, appear to behave differently to other cases of nephritis in that diuresis is not so marked a feature of the test, and examination of the specimens passed at the third hour do not show any difference in the urea percentage from that obtained at the second hour. Again it has been the custom to estimate the percentage of urea in the specimen passed before the urea is given with similar results. It would appear that since there is no evidence of urea retention in these cases, and the excess of urea is only slowly disposed of, that this excess is distributed throughout the body fluids and passes into the liquor amnii and the body fluids of the fœtus. At present we have no proof of this assertion, but it provides an explanation of the otherwise conflicting results obtained in nephritis of pregnancy. The observations made and the conclusions to be drawn from the work described in this paper are regarded as in a preliminary stage. A much larger statistical record is necessary before it can be said that the tests described are sufficiently reliable to warrant their application in every case of albuminuria in pregnancy. The results, however, show that the scheme of procedure adopted has yielded results which have been of value for diagnosis and prognosis, and sufficient to justify their application in as many cases as possible. Fortunately, toxæmias

of pregnancy are of comparatively rare occurrence, but if it can be shown that cases presenting features which resemble this condition can be differentiated by means of renal function tests the value of the latter is considerably enhanced.

The tests can be used both for diagnostic and prognostic purposes provided their individual and collective worth is fully recognized. The clinical study of such cases is, of course, of the first importance, and the object of this paper will have been achieved if it can be satisfactorily demonstrated that the tests are of real value to the clinician. This can only be accomplished as the result of co-operation and widespread application by combined effort. The work has been carried through with this objective, but at the same time the ætiology and causative factor or factors concerned in the toxæmias of pregnancy has not been lost sight of. The nature of the toxin or toxins is still unknown, but every piece of work adds another link to the chain of evidence leading to the final goal.

Conclusions.

1. The application of tests for renal function yields results which are of diagnostic value in albuminuria of pregnancy.

2. In the toxæmias of pregnancy the most reliable test is the diastase estimation in the urine which gives results considerably higher than those usually regarded as normal.

3. The ratio of albumen to globulin in the urine also provides data of diagnostic import in the toxæmias of pregnancy when albuminuria occurs.

4. The results obtained in toxæmias of pregnancy suggest that the toxin or toxins is present in the maternal blood, and exerts its primary effects on the blood vessels producing in the case of the kidney an acute glomerulitis or nephrosis.

5. The four tests applied, viz., diastase in the urine, the ratio of albumen to globulin in the urine, the urea content of the blood, and the urea concentration test have been found to give considerable information as to diagnosis and prognosis in cases of nephritis in pregnancy.

6. The tests must be carried out according to scheme, and the results interpreted collectively, as no single test is found to give sufficient data in assessing the amount of renal damage in nephritis in pregnancy.

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A Comparison between Ovarian "Hypernephroma" and Luteoma and Suprarenal Hypernephroma, with Comments on Suprarenal Virilism.[1]

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NEARLY forty years ago Grawitz propounded the theory that certain characteristic renal neoplasms were developed from misplaced remnants or "rests" of the suprarenal cortex, now called "accessory" suprarenals; these neoplasms were subsequently named "hypernephromas."

Hypernephromas have also been recorded in other localities where accessory suprarenals occur, or are believed to occur—such as the liver, the retroperitoneal tissue, the pancreas, the broad ligament, and even in the ovary and on the testicle.[2]

Peham (1899) described a large solid yellow tumour of the ovary, which on account of its macroscopic and microscopic appearances, and the supposed occurrence of suprarenal cortical tissue in the ovary, he called "hypernephroma"; several other cases have since been published.

In the last few years, however, the ovarian "hypernephroma" theory has been abandoned by many authorities who regard these tumours as derived from lutein cells, or at least not from suprarenal cortex.

Only two recent British textbooks of gynæcology refer to such tumours. Dr. Blair Bell (1910), alluding to congenital inclusions which may give rise to neoplasms, states that "on section some are seen to show a structure like that of the adrenal gland," but he observes that "cellular hyperplasia of the lutein layer has been

1. Received Sept. 1920 (Editor).

2. Accessory suprarenals rarely contain *both* cortex and medulla; they are usually situated in the interior part of the solar plexus at a little distance from the suprarenal gland. (Lucien et J. Parisot, p. 84). Professor Keith is of the opinion that "accessory suprarenals of the cortex in the mesenteries of the ovary and testicle are so common, that they should be regarded as normal and not errant bodies" (private communication).

mistaken for a growth of this nature." Dr. H. Williamson (1917), discussing malignant tumours composed of cells resembling those of the corpus luteum, does not commit himself as to their origin, but simply states that three views have been held, "(*a*) that the tumours arise from aberrant suprarenal glands, (*b*) that they arise from the corpus luteum, (*c*) that they arise from the interstitial cells of the ovary."

In 1919 Dr. Knyvett Gordon described in the *British Medical Journal* two cases of ovarian "hypernephroma," each measuring $1'' \times \frac{1}{2}''$ in diameter, and alluded to a third case. His diagnosis was challenged by Dr. Leith Murray in a letter to the same Journal; then after private correspondence, a histological report on the three specimens was furnished by Professor Turnbull of the London Hospital, giving three reasons why these tumours showed the main differential characters of lutein bodies, viz.: "(1) the stellate core of fibrin or granulation tissue, (2) the absence of clearly defined acini, and (3) the alternation of centrifugal and centripetal trabeculæ."

Dr. Knyvett Gordon, with the scientific man's love of truth, then admitted in a further letter to the Journal that his "original diagnosis was wrong."

Thus it is now generally recognised that ovarian "hypernephromas," or at least the smaller and more typical ones, have a closer resemblance to lutein formations than to suprarenal cortex.

There are, however, several additional reasons—which have escaped the notice of critics—why it is exceedingly doubtful if a single case of genuine ovarian "hypernephroma" has yet been recorded.

1. ***Embryological.*** Suprarenal cortical tissue is frequent in the broad ligament, yet there is no proved case of its presence *in* the ovary. This is corroborated by the fact that though such tissue is frequently found near or in the epididymis, and very rarely in the corpus Highmor, there is no proved case of its presence *in* the testicle.

2. ***Histological.*** The large ovarian "hypernephromas" are unlike the large[1] primary, and usually malignant, growths of the cortex of the suprarenal gland itself—called in this paper suprarenal hypernephromas; but they are usually, both clinically and structurally, like other large tumours described as lutein growths.

3. ***Clinical.*** The large ovarian "hypernephromas" are not associated with the changes in secondary sex characters, as hirsutes, etc., which are so frequent with suprarenal cortical tumours in young children, especially girls, and in women before the menopause. These sex changes never occur with lutein tumours.

1. "Large" to distinguish them from the adenoma, which is small.

On the other hand *one* of the much rarer hypernephromas of the broad ligament—a locality where accessory suprarenals are common—produced changes in sex characters, and histologically this appears like a true suprarenal hypernephroma.

1. Embryological.

A.—*There is no proved case of an accessory suprarenal* in *the ovary, but it is comparatively common in the vicinity.*

Accessory suprarenals in the broad ligament or its immediate neighbourhood have been described by Chiari (1884) in both broad ligaments of a woman aged 48, the left in the free margin under the ovary, the right above the spermatic plexus, between it and the parietal peritoneum—the size of a hemp seed or less; and in a woman aged 30 underneath the right kidney—the size of a pea, in both cases all three cortical zones were present: by Dagonet (1885) in a woman aged 32, under the right ovary—the size of a split pea: by Michael (1888) in the right broad ligament of an old woman, 2 inches in diameter: by Marchand (1883), six cases in fœtuses or very young children—in one case two cortical layers were present: by Marchand (1891), three cases; the first in the right broad ligament of a pseudo-hermaphrodite aged 50, it was the size of a testicle but showed no layers in the cortex, or medulla—there was also cortical hyperplasia of both suprarenals; the second the size of a hemp seed in a woman with amyloid degeneration; the third in the wall of both broad ligaments of a woman with cancer of the right ovary: by Ulrich (1895), 3 cases; the first (S. No. 16, 92) in a neonata perforata—here accessory suprarenals were found *close to* both ovaries, that on the left 4 mm. broad was situated 3 mm. above and somewhat lateral to the left end of the ovary and 5 mm. from the vena spermatica interna—both had more than one layer; the second case (S. No. 141) in a child 14 days old, 2 cm. thick, on the left vena spermatica 1 cm. above the ovary; the third (S. No. 43) in a child 3 years old just above the left ovary on the spermatic veins: by Targett (1897) in a fœtus, there being a distinction between "cortex and medulla": by Pilliet and Veau (1897), in the middle of the broad ligament of a women aged 21: by Gottschalk (1898), in a woman aged 28, on the under "cranial" surface of the suspensory ligament of the ovary: by Rossa (1899), in two new-born infants, in one case there was a central and peripheral zone: by Meyer (1898), seven cases in fœtuses or young children—they were small, being up to 3 mm. in diameter: by Weiss (1898), in the right broad ligament of a girl of 17, verified microscopically: by Scott Warthin (1900), in a woman aged 19, the size of a pea behind the ovary near the plexus veins—there was a cortex and a medullary portion: by Pick (1901), in a woman aged 40, the size of

a walnut, at the bifurcation of the iliac artery : by Lecène (1908), in a woman aged 37, the size of a millet seed, in the left broad ligament immediately under the point where the spermatic veins enter the mesosalpinx—layers were present : by Alamartine (1912), in a woman aged 60, the size of a lentil, in the left mesosalpinx under the tube : by Hepner (1870, quoted by Neugebauer), in each broad ligament of a female infant pseudo-hermaphrodite—they were a few millimetres long, and two cortical layers were present.

Sixteen observers have therefore described 34 cases of accessory suprarenals in the broad ligament or its vicinity. Twenty occurred in the very young and fourteen in adults; but in only one case, viz. Ulrich's No. 16, were they found *close to the ovary*. The fact that these bodies usually had two or three layers is additional histological evidence of their suprarenal cortical origin. Some observers however, like Warthin and Targett, have described the pigmented inner layer as medulla. This, however, is very improbable, for most embryologists believe that "the cortex and medulla are certainly of different origin," the former arising from "the endothelium covering the Wolffian ridge" and the latter "from the groups of cells which form the sympathetic ganglia." Aichel, however, still maintains that both cortical and medullary parts arise from the mesothelial cells over the Wolffian ridge (see Keith, 1913).

In addition to the 34 cases already recorded, Rossa described four and Pick three cases of small nodules in the broad ligament of adults, which they regard as imperfectly differentiated, or retrogressively metamorphosed suprarenals, on account of their microscopical character. The former believes they originate certain subserous cysts lined by epithelium.

Accessory suprarenal IN *the ovary*. It has often been assumed that suprarenal cortical tissue has actually been demonstrated in the ovary. Williamson (1917) admits that aberrant suprarenals are rare in this situation, for he says "they are seldom found in the ovary proper," while Alamartine (1912) remarks they may occur in the middle of the ovary. But neither of these writers give a single specific instance. The rarity of accessory suprarenals in the ovary is demonstrated by the fact that Poll (1906), in an exhaustive list of accessory suprarenals, tabulates as "present in the ovary ?" the cases of Lodi and Marchetti, and that Professor Robert Meyer (1912) in an elaborate paper on embryonic cell inclusions mentions none; Vonwiller (1911) cites Varaldo (1904) as giving the *only cases on record*. Varaldo, however, described three "rests" about 5-7 mm. each in diameter in the ovaries of *three women* aged from 31 to 41 ! The "rest" was always associated with a cyst, though in two at least this cyst was said to be separated from it by a narrow strip of ovarian tissue.

Marchetti (1904) also describes two very small "rests" composed of zona fasciculata only, in the ovary of a woman (age not given) which also contained a fairly large cyst lined by flattened epithelium; one rest lay upon the cyst wall, the other at a little distance from it.

Lodi (1902) publishes the following under the heading of "aberrent germs of suprarenal capsule in the ovaries."—"In the ovary of a woman 14 times pregnant who had hysterectomy and double ovariotomy were found nodules varying in size from a pea to a hazel nut, independent of the ovarian tissue." Microscopical examination revealed a capsule of connective tissue, rich in vessels sending septa towards the inside. Among the septa were columns of polyhedral vacuolated cells separated from one another by delicate capillaries. "Towards the centre of the nodule the septa tended to blend and lose themselves among *large masses of fibrin containing empty spaces*" (italics mine).

Now "accessory suprarenals" in the ovaries of *adults* must be viewed with great suspicion on account of their similarity to lutein formations—especially when they are associated with cysts or fibrin.

It has already been noted that of 34 cases of accessory suprarenals in the broad ligament and its vicinity, 14 occurred in adults and 20 in the very young. But the difference in relative frequency at the two ages is even greater than the figures indicate, because it required 11 observers to record the 14 cases in adults but only 6 observers to record the 20 cases in the young.[1]

There is additional evidence that accessory suprarenals are more frequently present in the very young. Hanau, quoted by Ulrich, in the course of 546 post mortems during four years found these bodies in 8 out of 116 young children (*i.e.* 6.9 per cent.), viz. 5 aged 1 to 14 days, 1 aged 4 months, and 2 in their third year; but he found *none in older individuals*. Wiesel, MacLellan, and Kirkbride respectively, had similar experiences with regard to accessory suprarenals in the neighbourhood of the testis (see later).

Clearly if accessory suprarenals are ever present in the ovary, they are most likely to be discovered in early life; besides, at this period they are unlikely to be confused with lutein formations.[2] I have only found one record of an alleged accessory suprarenal in a child's ovary, viz. Jessup's (1913). It was from a new-born baby and was exhibited at the New York Pathological Society. Jessup says "section of one of the ovaries shows a circular group of cells lying in the cortex which from their individual structure

1. 17 observers, not 16, because Marchand found them in adults *and* children.

2. Roger Williams states that "corpora lutea and recent ovarian cicatrices" have been discovered in the ovaries of newly-born infants, see later, p. 51.

and grouping in cords gives the picture of adrenal tissue. The cells in the periphery have a compact round nucleus and a smaller darker stained cell body than the cells of the central portion. They lie in rows or cords, one to three cells deep, which lie parallel to the circumference. Compared with the suprarenal of a new-born child they resemble the cells of the zona glomerulosa while the cells of the central portion are like those of the zona fasciculata. The cords of the latter run in various directions. There is a rich network of capillaries lying between the cords." Dr. Frank examined Jessup's specimen and stated " I do not think there is any question as to its interpretation." This histological description is rather incomplete, no lipoid was demonstrated, there are no drawings or photographs, and in the absence of a report by other pathologists, this apparently unique case must be regarded as not proven. On the other hand the tumour may have been a corpus luteum (see reference to Roger Williams, p. 51).

B.—*There is no proved case of an accessory suprarenal* IN *the testicle—apart from very rare ones in the corpus Highmor; but it is comparatively common in the vicinity.*

The absence of a proved case of an accessory suprarenal in the ovary is *corroborated* by a similar absence in the testis. But accessory suprarenals on the spermatic veins, near or on the testis itself, have been described by Chiari (1884), in a man aged 34, two fingers breadth below the right kidney, it showed a layered cortex; in a man aged 23, 3 cm. below the right kidney—both were near the spermatic veins: by Dagonet (1884), in the epididymis of a 28 days' old child, two cortical layers were present: by Roth (1888), quoted by Ulrich, in the corpus Highmor of both testicles in a case of Addison's disease: by Michael (1888), three in the new-born or young children and four in adults—six being on the right side and one on the left: by Lockwood (1900), in the inguinal canal of a boy—cortical layers were present: by Meixner (1905) in a new-born male pseudo-hermaphrodite, two small nodules near the right and one near the left testicle—all contained the three cortical layers: by Robert Meyer (1912), three cases in the new born. Meyer (1911) quotes Weiller, d'Ajutolo, and Friedland as describing " rests " on the spermatic cord, Pilliet, Regand and Loisel as describing " rests " between the testicle and epididymis. Kirkbride (1911) examined 2,000 sections of 54 specimens of testis, epididymis and spermatic cord from new-born infants, a variety of embryonic disturbances was observed. Circumscribed structures, " most of which should be classed as accessory adrenals," were found in eight, " one lay in the epididymis among the efferent ducts, five near the testis or epididymis and two near the vas deferens."

Wiesel (1898) demonstrated that accessory suprarenals were more common in *young* males; he found them near the vas, epididymis or testis in 76 per cent. of 15 new-born males, whereas in an equal number aged 1—60 he sometimes found "cell columns and heaps which might be retrograde adrenal rests." Typical ones were found in two cases among the terminations of the "tubules" of the epididymis. MacLellan (1919) had a similar experience, for in about 660 operations for radical cure of hernia in male children; he found suprarenal nodules on the hernial sac in approximately one per cent—a photo-micrograph of a typical nodule obviously suprarenal cortex is given—but he had "not yet observed an adrenal rest in an *adult* hernia, though the cases have not been so numerous."

Accessory suprarenal IN *the testicle.* There is only one record of an alleged accessory suprarenal among the seminiferous tubules, viz. Robert Meyer's (1912) specimen No. 228, in the undescended testicle of a new-born child. A drawing shows a nodule under the capsule among the seminiferous tubules consisting of large epithelial-like cells without any arrangement suggesting different cortical layers. There is no mention of lipoid, and no histological description whatever. This case must be regarded as not proven.

2. HISTOLOGICAL.

A.—*The large ovarian "hypernephromas" are unlike the large primary growths of the cortex of the suprarenal gland itself.*

Ovarian "hypernephroma" may be divided into two subgroups:

(*a*) small tumours, an inch or less in diameter—of no clinical importance—which are *now* generally recognised as of lutein origin;

(*b*) large tumours, perhaps the size of a fœtal head, which produce severe clinical effects and are usually fatal; their resemblance to the corpus luteum is comparatively slight. These are the tumours subjected to criticism.

I have collected fourteen such "hypernephromas," eight in the ovary, and two in the broad ligament—apparently originating in the ovary; also four others in the broad ligament apparently not originating in the ovary, which will be considered later. All these cases have been abstracted below and photographs of the original illustrations given. With certain exceptions to be alluded to presently there is no essential clinical, macroscopic or microscopic difference between them.

A.—*Ten cases of large ovarian "hypernephromas."*

Case 1. Peham (1899). A woman who had had four children, the last eight years ago—age not stated—complained of pain, menstrual irregularity

and abdominal enlargement. The right ovary was removed; there was a cyst in it containing 2,800 cc. of hæmorrhagic serous fluid. The solid part of the tumour—the size of a child's head—was on the edge of the cyst. It was made of large yellow nodules with soft red centres and surrounded by fibrous tissue. Two small cysts were present—probably from necrotic changes. Microscopically the tumour was composed of vacuolated epithelial-like, sometimes multinucleated, cells, containing glycogen; fat is not mentioned. These cells were usually polygonal, but occasionally cubical when arranged to form gland-like lumina. Many capillaries were present on to which the epithelial cells abutted. (See Fig. 1: note the clear cytoplasm, and compare with Figs. 13 and 15.)

The patient recovered after the operation. The author regards the growth as hypernephroma developing on the wall of an ovarian cyst.

Case 2. Peham and Paultauf (1899). A woman, aged 50, complained of pain in the stomach and vomiting. The right ovary was removed for a tumour 15×10×9 cm. There was a second growth in the region of the stomach. Macroscopically the tumour was encapsulated. It was made of a small cyst and three large nodules with a radial arrangement at their periphery. The colour was red or yellow. Microscopically the appearances were similar to the first case, the vacuolated cells were also arranged round capillaries, but lumina are not mentioned. Glycogen was present. (See Fig. 3).

The patient died of metastases three months after the operation. There was no post mortem

Case 3. Sternberg (1906). A woman, aged 18, unmarried, had a laparotomy. Two very cystic tumours were removed; one—the size of a man's head—originated in the ovary, the other—somewhat smaller—was found in the broad ligament and was regarded as a metastasis. Macroscopically they varied from pale yellow to red with numerous areas of mucoid transformation. Microscopically they were composed of cubical cells, usually vacuolated, and frequently arranged round capillaries to form cell mantles—occasionally gland-like or tube-like structures were present. Glycogen was demonstrated. The cysts were of degenerative origin. There is no further clinical information.

Case 4. Scudder (1907). A woman, aged 40, with three living children, complained of amenorrhœa and emaciation. Laparotomy revealed "on the side of each ovary a mass, two inches in diameter, papillomatous in appearance." There was "encysted peritonitis" and "numerous white opaque spots, the size of a pin-head, upon the peritoneum of the intestines"; these were regarded as disseminations from the ovarian tumours. Nothing abnormal was felt in the liver. Microscopically the ovarian tumours were composed of nests of cells "having in some places a glandular arrangement and in other places being arranged in columns separated by a small amount of fibrous tissue. The cells were large, with rounded nuclei and considerable protoplasm which, in some, showed fatty degeneration. Occasionally the cells were in large masses and showed a smaller amount of protoplasm." The diagnosis was hypernephroma. The patient died nine months after the operation.

Case 5. Gaudier (1908). A girl, aged 4, whose breasts and external genitals were those of an adult, had for three months suffered from menorrhagia and metrorrhagia, simultaneously an abdominal swelling appeared. The left ovary was removed for a pedunculated tumour the size of a very

large orange. Macroscopically it was yellow and surrounded by a fibrous capsule which sent vascular trabeculae into its substance—one part was covered by ovary. The microscopical sections were examined by Professors Laguesse and Curtis. The tumour cells were polyhedral and contained fat. After considerable difficulty they decided it was "*very probably a hypernephroma and not a lutein tumour*," partly because the characteristic buds of vascular connective tissue dividing the polyhedral cells into large compartments were absent—instead the compartments were slender and like those of the adrenal cortex—and also because very occasionally the cells were arranged in hollow epithelial columns resembling uriniferous tubules, like those Grawitz had described in "hypernephroid tumours of other organs." It is important to note, however, that one of these "tubules" contained loose cellular elements.[1]

Case 6. Rosthorn (1909). A woman, aged 27, primipara, complained of pain in the abdomen and loins. Both ovaries were removed for nodular tumours, one being the size of a man's fist, the other of a man's head. Macroscopically there were yellow, and also necrotic or mucoid areas, and some cysts embedded in a ground substance of very vascular fibrous tissue. Microscopically "they resembled Pick's case,"[2] the growth consisting of epithelial-like cells infiltrated with fat, lying directly on a fine capillary network: glycogen was present. The cysts were apparently due to degeneration.

1. Alfred Gallais (*Le Syndrome Genito-surrenal*, Vigot Frerés, Paris, 1914, pp. 1—424), in a collection of cases of children with suprarenal hypernephromas and changes in the sex characters, quotes as **Observation** XXVII A. Debeyre et O. Riche—Surrenale accessoire dans l'ovaire (*Soc. de biol.*, Paris, 21 decembre 1907, p. 733), and as Observation XXVIII Gaudier's case. *These two cases are the same case.* Debeyre's account was published five months before that of Gaudier. It describes an accessory suprarenal in the ovary of a girl aged 4 which was removed for supposed sarcoma—the name of the surgeon is not given.

The clinical descriptions are practically identical. Thus in the former we read: "Sur le mont de Vénus, le système pileux est très développé; les petites lèvres, fortement pigmentées, dépassent les grandes lèvres; les seins offrent un développement remarquable L'aréole a pris une teinte brunâtre; une série de tubercules de Montgomery apparaissent sur la surface, et le cercle veineux périaréolaire est très net." In the latter we read: "Système pileux du mont de Vénus est très développé, les petites lèvres fortement pigmentées dépassent les grandes lèvres. Les seins offrent un développement remarquable vu l'age du sujet. Ils présentent une forme hémisphérique et l'aréole a pris une teinte brunatre, sur la surface d l'aréole une série de tubercules de Montgomery très apparents; le cercle veineux péri-aréolaire de Haller est très net."

The microscopical descriptions are also practically identical; for example, we read in both, of a certain portion of the tumour resembling urinary tubules, one of which contained elements "qui dissociés, semblent nager dans la lumière!"

Gallais makes exactly the same mistake over a case of hypernephroma in a woman. He gives, under Observation XLI, Linser's account of a suprarenal tumour from the Catalogue of the Royal College of Surgeons, England, in an epileptic woman, aged 32. Under Observation XLVI he gives Davis' description (*Lancet*, Oct. 3 1896, p. 944) of a suprarenal tumour in an epileptic woman, aged 32, "which was presented to the Royal College of Surgeons, England."

2. Ill-formed lumina are not mentioned—though they were present in Pick's case, see Case 9.

The patient died a short time afterwards with metastases in the spinal column. There is no mention of a post mortem.

Case 7. Vonwiller (1911). A woman, aged 27, who had only menstruated three times in 17 months after the birth of her first child, complained of abdominal pain. A tumour, the size of a fist, was removed from the right ovary. Macroscopically it was encapsulated and lobulated, and red, yellow or white. There was one very small cyst in a necrotic area. Microscopically it was composed of columns and groups of epithelial-like cells rich in fat, lying in a stroma of capillaries or sometimes large blood spaces. Glycogen is not mentioned. Gland-like structures were absent. The cyst was due to degeneration (see Fig. 4; note the clear cytoplasm). There is no further clinical history.

Case 8. Santi (1906) described a hypernephroma of the ovary and kidney. A very obese woman of 53, formerly menstruated regularly, but for the last six years she suffered from metrorrhagia and the abdomen gradually enlarged. An intensely yellow tumour of the right ovary, the size of a fœtal head, was removed, as well as the uterus containing an intramural fibroid. The patient died of shock. At the post mortem the left kidney contained an encapsulated white yellow growth as big as a fist: other growths are not mentioned. Microscopically the kidney tumour was composed of cubical, polyhedral, or cylindrical cells with small round nuclei and translucent (vitreous) or finely reticulated cytoplasm. Fat was demonstrated. The cells were arranged in alveoli or perivascularly: sometimes they formed "sort of canals," the ovary had the "same microscopical appearances," but was more vascular.

This case is undoubtedly one of an ordinary renal "hypernephroma" with its characteristic clear cytoplasm, producing a metastasis in the ovary.

A.—*Broad ligament "hypernephromas" apparently originating in the ovary.*

Case 9. Pick (1901, No. 5). A woman, aged 51, with three children—the last born 19 years before—complained of abdominal pain and uterine prolapse; for the last year her periods were usually every three weeks and the flow scanty. The right broad ligament contained a tumour 9×7.5×7.5 cm. adjacent to the ovary, which the author believed *arose in the ovarian hilum*. Macroscopically it was soft, grey, red, or yellow; towards the periphery there were many degeneration cysts filled with clear or blood-coloured fluid, the centre was necrotic. The right ovary contained a small metastasis. Microscopically the tumour was composed of approximately polyhedral cells with translucent cytoplasm; many contained fat, glycogen or pigment. They were usually arranged in solid alveoli—though sometimes in the peripheral cystic areas in gland-like lumina—surrounded by a delicate network of capillaries (fig. 2). The patient died two years after the operation with metastases in both kidneys, the left suprarenal and cerebellum.

Case 10. Gardner and MacCleary (1908). A woman, aged 49, a nullipara, who had not menstruated for eight years, complained of abdominal pain and swelling. A large nodular tumour with several cysts which had "presumably arisen from the ovarian hilum"—for no trace of ovary was found—was removed from the left broad ligament; it was not examined. Eleven months later a "very similar mass"—but apparently solid—

measuring 10×13 cm., was removed from the same region. Microscopically the denser parts were composed of columns of epithelial cells with relatively large nuclei and a narrow rim of cytoplasm embedded in a vascular stroma—the appearances recalled the adrenal cortex. In the more succulent parts the cells were much larger—the scanty cytoplasm giving the cell an "empty look"—and were arranged in alveoli in a stroma of blood and lymph vessels. No fat is mentioned. The appearances here were identical with a " hypernephroma of the kidney " (see Fig. 5; note the clear cytoplasm). As no ovarian tissue could be found in sections from various parts of the tumour " it was impossible to say whether the growth began in the ovary or broad ligament." Two years later the patient was in " good health."[1]

Summary.

It emerges from the descriptions of these nine different observers, that the large ovarian "hypernephromas" are solid yellow tumours, which usually contain hæmorrhagic and necrotic areas, and sometimes a few degeneration cysts. They were called " hypernephromas "—apart from incorrect embryological reasons—not only on account of their yellow colour, and perhaps the presence of fat, glycogen or lumina; but particularly on account of the general resemblance of the groups of clear or very vacuolated cells lying in a capillary stroma, *to the zona fasciculata of the suprarenal cortex when loaded with " fat."*[2] Further their general macroscopic and microscopic resemblance to the so-called renal " hypernephroma," was regarded as strong additional evidence of their suprarenal origin.

The structure of the true suprarenal hypernephroma.

Apart from the small adenoma, primary neoplasms of the cortex of the suprarenal gland are very rare. But I have had the good fortune to examine sections of 9 undoubted cases of true hypernephroma, viz., Dun's, Ritchie's, French's and Turnbull's in young girls, Adam's in a boy, Hewetson's in a woman of 44; also two in men, viz. from Mr. Thelwall Thomas, Liverpool Royal Infirmary, from Dr. Kettle, St. Mary's Hospital, London, and one in a woman from Dr. Spilsbury, London. I am greatly indebted to these gentlemen for kindly lending me their sections. (See Figs. 16–29.)

The first six were associated with changes in the sex characters, and have already been published elsewhere (see Glynn, Lit. 1912, and Turnbull, 1920), the three others are described below.

1. Perhaps this case should be put in the group of broad ligament " hypernephromas " apparently not originating in the ovary, and its place taken by Case 3 of that group (see later).

2. For a more detailed analysis see page 41.

Case 7 (Kettle), a male, aged 37, died of perforated duodenal ulcer, Both suprarenals were lobulated and hæmorrhagic, and measured about 3 inches by 1 inch; but these lesions produced no symptoms. The tumours evidently originated from the suprarenal cortex, not only because no primary growth was found, but also because both had the usual characteristic microscopic structure, and in one there was a gradual transition from the normal suprarenal to the neoplasm. (See Fig. 20.)

Case 8 (Thomas), A.S., male, aged 37, complained of headaches for about a year and recently of abdominal pain. "The chest, arms and legs were covered with hair." A large swelling was found in the left hypochondrium, though the patient himself had noticed nothing. He died three days after an exploratory laparotomy. Post mortem there was a large slightly lobulated, encapsulated tumour, roughly resembling the shape of the adrenal, lying on the top of the left kidney. This weighed $4\frac{3}{4}$ lbs., measured 10 inches in its longest diameter, and on section was whitish with numerous hæmorrhages. The suprarenal on this side could not be found. The other organs were normal. (See Fig. 23.)

Case 9 (Spilsbury). This was removed by operation from a woman, age unknown, in 1912. "The surgeon was certain it was from the suprarenal for the kidney was not invaded, but he could recall nothing more regarding the case." (See Fig. 26.)

Photomicrographs of these nine tumours are shown (Figs. 16—29). It is unfortunate that they have been fixed and stained by different methods, and that as a rule only one section of each is available. I have also reproduced in Fig. 30 some drawings from a paper by Woolley and Adami of "A primary carcinomatoid tumour (mesothelioma) of the adrenals, with sarcomatous metastases" in a man of 42.

A survey of the literature of primary neoplasms of the suprarenal cortex reveals a great confusion in the nomenclature. Apart from the small adenoma, they have been called malignant hypernephroma (Kaufmann), alveolar sarcoma (Beneke), perithelioma (Rolleston and others), malignant adenoma (Ribbert), suprarenal epithelioma (Marchand), hypernephroid tumour (Lubarsch), mesothelioma (Woolley and Adami), etc.

This confusion is the result of the great variation in the histological structure. Thus Rolleston and Marks say "our own impression is that malignant tumours of the suprarenal bodies are peculiar, and form a special class. They may approach structurally either the carcinomata or the sarcomata, and sometimes one and the same tumour may and in different parts resemble both." Woolley and Adami also emphasize the various types of cells seen in these suprarenal tumours. (See Figs. 19 to 24.)

The variation in the microscopical appearance of these tumours may be explained as follows: The specific cells of the suprarenal cortex are developed from mesothelium, which is in turn developed from mesoblast, and, as Woolley and Adami have pointed out, it

is quite natural that in a markedly anaplastic growth from such tissue, the epithelial (*i.e.*, mesothelial) characters and arrangement of the cells should revert to a more primitive sarcomatous (*i.e.*, mesoblastic) type.[1]

Perhaps some of the variation is due to development of the tumour from two or even three cortical layers—there is no evidence at present that the medulla ever participates.

The photographs 16—30 illustrate many of the characteristic features of the suprarenal hypernephroma, among others the following:—

(1) In almost all the cases there is a great variation in the tumour cells in the same field, or in different fields of the same section, or between the primary growth and the metastasis. It will be noted that the cells are as a rule round, oval or polyhedral, but may be spindle-shaped, oblong, rectangular or very irregular. Their size is usually about 20μ, but giant cells of from 40μ to 60μ occur (see Fig. 22). Though the nuclei are usually small and round or oval with a well marked nucleolus, there are almost always a few and often many cells with pyknotic or large irregular hyperchromatic nuclei; sometimes two or more nuclei are present (see especially Figs. 20, 21, 22, 23, illustrating five tumours).

The cell cytoplasm may be a little vacuolated (Fig. 21)—perhaps partly depending on the fixative used—but it has not the clear or very vacuolated appearance so characteristic of the adrenal cortical cells when loaded with "fat," and the majority of the cells of the ovarian "hypernephroma" and the renal "hypernephroma." (See Figs. 14, 1, 2, 4, 5, 13 (1), and 15.)

The tumours from Ritchie's, Dun's and Turnbull's cases in girls with sex changes, and Kettle's, in a man with no such changes, are practically identical (see Figures 17, 19, 21, 22, 20); whereas Hewetson's tumour in a woman with sex changes, and Spilsbury's are very similar, though the variation in the cells is slight (see Figs. 18 and 26).

(2) A great variation in the amount of connective tissue stroma. This is even greater than obtains in scirrhus and medullary cancer of the breast, because in some sections (see Figs. 17, 20, etc.) no stroma is visible with the ordinary hæmatoxylin stain. There is no essential difference, however, between tumours with much

1. The term "suprarenal hypernephroma," used throughout this paper, has the following advantages: 1. It indicates the origin of the tumour, and distinguishes it from the "renal hypernephroma." 2. It does not postulate a malignant tumour, some suprarenal hypernephromas are "innocent." 3. It does not raise the difficulty of deciding whether the tumour histologically resembles a carcinoma or sarcoma; but it clearly distinguishes it from the only other common primary malignant tumour of the suprarenal, viz. the neuroblastoma or gliosarcoma of the medulla.

connective tissue stroma and those with apparently none, because even the few sections available demonstrate a gradual transition between the two types; for instance, the section of Adams' tumour of a boy with sex changes almost exactly resembles a badly-fixed portion of Hewetson's tumour, a woman with sex changes (see Figs. 25, 1 and 2). Again, the very dense stroma present throughout Thomas' case of a man with no sex changes, resembles a portion of Dun's tumour near a fibrous septum, from a girl with sex changes (see Figs. 23 and 24).

The different types of cells present in the nine tumours closely resemble some of those illustrated by Woolley and Adami (see Fig. 30).

(3) In French's tumour, a girl with sex changes, there is a rather unusual perivascular arrangement of the tumour cells, partly or wholly due to necrosis—misnamed by some writers "perithelioma." This perivascular arrangement does not indicate a different type of tumour, for a somewhat similar appearance is found in a portion of Turnbull's tumour, also due to necrosis (Figs. 27 and 28); while higher power photographs of the wall of a small vessel in both tumours are almost identical (Fig. 29, 1 and 2). But most important of all, the metatasis of French's tumour which consists of small cells (very like others present in a portion in the primary growth of Spilbury's case (see Figs. 16 and 26 (2)) shows no perivascular arrangement, because there is no necrosis.

Lumina. The presence or absence of lumina demands special consideration. For many years pathologists, accepting without question Grawitz's theory that the ordinary primary more or less yellow renal neoplasm is a " hypernephroma," have also, because well formed gland-like *lumina are very common* in these tumours,[1] assumed that even ill-formed pseudo-lumina in a given tumour is evidence of its suprarenal origin. The Grawitzian theory, however, has been vigorously attacked by Sudeck (1893), Stoerk (1907), Zehbe (1910), Wilson and Willis (1911), Glynn (1911), Dunn (1913), and others. Dunn has pointed out that " certain papilliferous cysts " frequently found in the kidney " are the most probable origin of tumours of the Grawitz type."

There is evidence that ill-formed pseudo-lumina are occasionally present in the human suprarenal cortex and in small adenomata developing there, Beckmann (1914). In the larger tumours " true lumina " have occasionally been described, as by Manasse (1896) (Case 25), also by Dobbertin (1900), though in the latter they were certainly pseudo-lumina due, as Ribbert believes, to the " destruction of the centre of cell masses." The majority of writers, how-

1. Zehbe, examining 37 cases, found lumina in 59·5%.

ever, as Woolley, Zehbe, Lasagna, etc., do not allude to any sort of lumina in these tumours.

There was no trace of lumina in the sections of the nine cases, except Kettle's, where an occasional ill-formed pseudo-lumen appeared—obviously produced by shrinkage.

It is remarkable how little the histological appearances of the hypernephroma are an index of its malignancy. Thus, French's tumour, which is moderately atypical, and Turnbull's tumour, which is very atypical, both produced metastasis in the lungs, whereas there were no metastases anywhere from Dun's and Ritchie's tumours, although they were apparently as atypical as Turnbull's.

The evidence at present available indicates that there is no real histological difference in these suprarenal hypernephromas, whether they occur in young or old, in males or females, with or without change in sex characters.

Comparison of the Structure of Ovarian "Hypernephroma" and Suprarenal Hypernephroma.

Macroscopical. The differences are slight. There is a marked tendency to hæmorrhage and necrosis in both types of tumour; but in the suprarenal group the yellow colour is not so frequently mentioned, and there is also an entire absence of cyst formation.

Microscopical. A comparison of the histological descriptions and the photographs demonstrates that the ovarian and suprarenal hypernephromas are quite unlike one another, though the former often resembles the so-called renal "hypernephroma" (see Figs. 13 and 15). The suprarenal hypernephroma differs from the ovarian "hypernephroma" especially in the great variation in the shape and size of the tumour cells and their nuclei, in the absence of the characteristic clear or very vacuolated cytoplasm, and in the almost complete absence of well formed gland-like lumina. *Whereas the resemblance of the ovarian "hypernephroma" to the suprarenal cortex is more or less close, the resemblance of the suprarenal hypernephroma itself to the cortex, is usually so slight, that none but an expert would suspect its origin.*

B.—*The large ovarian "hypernephromas" are usually like the large "lutein" tumours, both clinically and structurally.*

Fourteen of these tumours have been collected. They are divided into Sub-group One—9 well recorded cases; Sub-group Two—5 briefly recorded cases.

B.—*Lutein Tumours (Sub-group One, 9 cases).*

Case 1. Voigt (1895). A woman, aged 30—who had had one child—when eight months pregnant complained of abdominal pain, swelling of

the legs, and ascites. The left ovary was excised for a tumour as big as an adult head, and two fœtuses were removed from the uterus. Macroscopically the tumour was soft and grey-yellow with a central necrotic and hæmorrhagic zone; a thick capsule full of blood vessels surrounded it, sending vascular septa into its substance. Microscopically it was composed of irregular heaps and columns of oval polygonal or rather spindle-shaped cells, separated from one another by large blood spaces. The majority of these cells resembled lutein cells; in others, however, the nuclei were larger and stained more deeply, and some were multinucleated. Vacuoles and fat[1] in the cytoplasm are not mentioned. There was much degeneration and, as the polygonal cells were often arranged round vessels, the tumour was regarded as a perithelioma of lutein origin. A lutein body was present in the right ovary, its cells resembling the tumour cells.

The patient died seven days after the operation with a large ulcer of the stomach and early bilateral hydronephrosis.

Case 2. Schaller and Pforringer (1899). A woman, aged 32, ix-para, was admitted to hospital with metrorrhagia, abdominal enlargement and pain. Both ovaries were removed, the left for a small ordinary cystic tumour which was not further examined, the right for a tumour measuring 11×9×4.5 cm. Macroscopically the latter tumour was of a coarse fibrous nature and contained an extraordinary number of small cysts, some full of blood. Microscopically it was composed of columns and cords of flat, epithelial-like cells between which capillaries were inserted—some contained fat droplets. The cysts were bounded by degenerated tumour cells or pigmented fibrous tissue. The tumour is described as cystic transformation of the corpora lutea with a local carcinomatous degeneration. (See Fig. 7.)

Twelve days after the operation a hydatid mole was expelled from the uterus. Four months later the uterus was normal.

Case 3. Santi[2] (1902). A woman, aged 25, with one child, complained of persistent metrorrhagia and abdominal pain. The right ovary was removed for a rapidly growing tumour, when she was three months pregnant. There was no trace of fresh corpus luteum in the left ovary. Macroscopically it was rather nodular and had a thin capsule which sent septa into its substance. Its centre consisted of a soft yellow-red brain-like mass dotted with blood extravasations. Microscopically it was like an alveolar sarcoma. There were two types of cells, the first, large of varying shape with copious cytoplasm and some multinucleated, the second smaller with scanty cytoplasm. The former were derived from the lutein cells. The latter were derived from proliferation of the connective tissue elements of the corpus luteum and developed into the fibrous stroma which surrounded islands of the larger cells. (See Fig. 9.)

The patient died six months later from metastases.

Case 4. Michelazzi (1902). A woman, aged 45, who had had three children, the last seven years ago, complained of a few months' amenorrhœa and later abdominal pain and swelling. The right ovary was removed for a solid tumour the size of a man's head. Macroscopically it was nodular, covered with a thick vascular fibrous capsule, dividing it into

1. The tissue was hardened in alcohol so fat would be dissolved.

2. See Santi, *Boll. della Soc. Tos. di Ost. e. Gin.*, 1902, No. 1; also Santi, *Monat f. Geb. u. Gyn.*, 1904.

lobules. The substance was " gray " with patches of old and recent blood extravasation. Necrotic areas were present but no cysts. Microscopically it was chiefly composed of small darkly staining " sarcoma " cells separated by a scanty inter-cellular substance; but " like Santi's Case 1," there were also zones, about the size of a corpus luteum, of larger round cells containing yellow pigment and big nuclei, which resembled lutein cells, and merged into the tumour cells at the periphery of the zones: hæmorrhagic areas were present in the centre of these zones. No complete corpus luteum was found. Thin-walled capillaries were numerous. Neither fat nor glycogen was mentioned. The patient recovered from the operation.

Case 5. Santi (1905, No. 2). A woman, aged 60, v-para, previously healthy, who had not menstruated since 45, complained of metrorrhagia for a few weeks. Total hysterectomy was performed. The left ovary was the size of a fist, nodular, firm and white with many large intensely yellow areas. Microscopically the white areas were composed of bundles of fibrous tissue, the yellow of groups of polygonal or round cells with a single round nucleus and slightly granular cytoplasm held together by inter-cellular substance: some of the cells were larger and showed mitotic figures. Much fat was present, but the yellow colour was partly due to pigment. Mast cells were noted. There were numerous capillaries and blood spaces lined by endothelium. The tumour was regarded as a " sarcoma luteinico." Santi does not compare this with his former case. There was a nodule in the uterus the size of a nut, arising from the connective tissue of the mucosa which proved to be a mixed-celled sarcoma; no fat was present. " The results of the operation were good."

Case 6. Grouzdew (1903). A woman, aged 60, pregnant 14 times, suffered ten years after the menopause from metrorrhagia and abdominal pain; both ovaries were removed, the right for a tumour the size of a large plum—it was a " kystoma proliferum glandulare "—the left for a large trilobulated tumour. Macroscopically the centre consisted of a solid yellow mass with small cysts, while the three peripheral lobules each contained one large cyst, two with some papillomatous growths. Microscopically it was composed of groups of moderately large irregularly formed cells with yellow pigment resembling " lutein cells " lying among relatively large vessels; the amount of connective tissue stroma varied (see Fig. 8). The cysts were lined by lutein cells, except one which was lined by cylindrical epithelium. In the centre of the tumour among the necrotic areas, the lutein cells were grouped around the remains of a corpus albicantium, from which they seemed to arise. The author regards the case as a " sarcoma ovarii cysticum lutein-cellulare " arising in a cystic ovary. On account of the woman's age he believed it arose from cells enveloping the corpus albicantium. The patient recovered from the operation, but after six months ascites appeared and the growth recurred in the pelvis; laparotomy revealed an irremovable pelvic tumour with metastases in the lymphatic glands and on the peritoneum. Microscopically the latter were spindle-celled sarcomata.

Case 7. Savage (1909). A woman, aged 38, iv-para, had abdominal pain, vomiting, emaciation, and ascites. Both ovaries were removed, the right for a tumour the size of a fœtal head, the left for one the size of a walnut. Macroscopically both tumours had opaque pale yellow, and also œdematous areas. Microscopically they were composed of large, round, oval, or polygonal cells with a small nucleus, often flattened against the

cell wall; the cytoplasm was either granular or translucent and vesicular; as " fat " could not be demonstrated with osmic acid the latter appearance was believed to be due to œdema.[1] The stroma was made of a reticulum of connective tissue. Vessels are not mentioned. (See Fig. 6, comp. Fig. 5.) Savage concludes that the tumour arose from an overgrowth of lutein cells, partly on account of its yellow colour and also from the resemblance of the cells to lutein tissue. The patient died from exhaustion $5\frac{1}{2}$ months after the operation: there was no post mortem.

Case 8. Christian (1910). A woman, aged 21, married, no children, complained of metrorrhagia for several months. A tumour was removed the size of an orange, which projected from the posterior surface of the right broad ligament and rested on the internal border of the ovary, being apparently fused with it. Macroscopically it was grey with yellow nodules, and a central cyst as big as a hen's egg full of clear fluid. Microscopically it was composed of epithelial cells which resembled lutein cells and contained xylol-soluble fat. There is no mention of blood vessels. It had the structure of an epithelioma and was regarded as " probably " originating from the ovary and from the corpus luteum. The patient left the hospital three weeks after the operation; her menstrual function became and remained normal.

Case 9. Massabuau (1913). A woman, aged 48, in whom menstruation had become irregular with some metrorrhagia, noticed a slowly increasing abdominal swelling. The left ovary was removed for a tumour the size of an orange; there was an inoperable growth in the pelvis. Macroscopically the periphery of the tumour consisted of pale yellow, circumscribed nodules; these projected into its centre, which contained many degeneration cysts, some full of blood and fibrin. Microscopically it was composed of irregular polyhedral cells with a vacuolated cytoplasm and round or crenated nuclei, like the " spongiocytes " of the suprarenal cortex; lutein was demonstrated by Sudan. They were grouped sometimes by fibrous tissue into alveoli, but mainly radially around blood vessels. The patient must have died as the pelvis contained an " inoperable growth."

B.—*Lutein Tumours* (*Sub-group Two, 2 cases*).

Case 1. Rokitansky (1859), quoted by Santi, 1904, described a lobulated tumour the size of a child's head in the left ovary of a woman of 65. It was covered with a thick fibrous capsule, the substance was convoluted, and reddish white and pale yellow. Microscopically it was an ovarian carcinoma of the corpus luteum. Fat was present.

Case 2. Maffucci (1882), quoted by Santi, 1904, described a " cystic adeno-sarcoma " of the ovary, which developed not only from the theca of the follicles and the connective tissue, but also from the corpus luteum, because he found in the middle of the tumour, yellow masses containing pigmented cells. Santi remarks that the examination was incomplete, and there is no evidence that the corpus luteum played other than a quite secondary part in the formation of the tumour.

Case 3. Wendeler (1899) described a tumour removed at operation from a woman before the menopause, which macroscopically resembled a giant corpus luteum; on microscopical examination it proved to be a sarcoma, probably derived from the corpus luteum. There are no details.

1. There is no information regarding the method of fixation.

Case 4. Martin,[1] quoted by Santi, 1904, very briefly describes a tumour having the appearance of a giant corpus luteum in the ovary of a woman before the menopause, which microscopically was a sarcoma.

Case 5. Ewing (1919), of Cornell University, described a solid yellow encapsulated tumour of the ovary measuring $2\frac{1}{2} \times 3\frac{1}{2}$ cm. which, macroscopically, resembled an enlarged corpus luteum. Microscopically "it was an alveolar sarcoma, the septa and cells merging insensibly. The cells were large and small, polyhedral, with clear or slightly granular cytoplasm, and dense borders." There is no clinical history.[2]

Summary of certain features usually present in the ovarian "hypernephromas"[3] *and the nine lutein tumours*—Sub-group One only considered unless the contrary is stated.

1. *Clinical.* (*a*) Age. There is no essential difference except that hypernephroma Case 5 was in a child of 4; three hypernephroma cases and two or three lutein cases had reached or passed the menopause.

(*b*) Pregnancies. Hypernephroma cases: former pregnancies, 4, ?, 3, 0, 1, 1, 3, 0; present, nil. Lutein cases: former pregnancies, 1, 9, 1, 3, 5, 14, 4, 0, ?; present, Cases 1, 2 and 3.

(*c*) Menstrual disturbances. Hypernephroma cases: amenorrhœa, 2 cases; "irregularity," 1 case; menorrhagia, 1 case. Lutein cases: amenorrhœa, 1 case; menorrhagia or metrorrhagia, 5 cases.

(*d*) Malignancy, *i.e.*, evidence at operation, or death from metastases. Hypernephroma, 5 cases; lutein, 4 cases, excluding Case 2, histologically "carcinomatous degeneration"; Case 4, "sarcomatous," and Case 8, "epithelioma." In some cases there is little or no after history given.

2. *Macroscopic.* There is no essential difference in shape, size, capsule, or tendency to regressive changes, *i.e.*, softening, hæmorrhage, or lastly cyst formation (see page 43). Yellow nodules or areas—almost invariably stated to be an important feature—were mentioned in all the seven hypernephroma cases carefully described macroscopically, and in all lutein cases except No. 4 where the colour was "grey." They were also mentioned in the five lutein cases of Sub-group Two.

Both ovaries were affected with primary growth in hypernephroma Cases 4 and 6, and in lutein Case 7.

1. Martin also mentions two cases were described by Klebs and Klobs respectively.

2. McIlroy (1909) briefly mentions an enormous solid ovarian tumour she removed, which a post mortem proved to be primary. Microscopically it was not like a sarcoma or an epithelioma. She thought it was "similar" to Dr. Savage's case and that "both belong to the class of peritheliomata."

3. Case 8A of the ovarian metastasis secondary to renal "hypernephroma," has been omitted from the general summary.

3. *Microscopic.* (*a*) There is no essential difference between the description of "hypernephroma" and lutein tumours as regards the shape and size of the tumour cells. In hypernephroma Cases 4 and 10, and in lutein Cases 1 ?, 4, and 5 a large and small type of tumour as distinct from stroma cell are specially mentioned. Hypernephroma Case 1 and lutein Cases 1 and 3 contained multinucleated cells. In the hypernephroma cases the cytoplasm of the tumour cells was usually clear, or contained many vacuoles or fat or both, except in Case 10 where it was "empty"; "fat" was demonstrated in Cases 4, 5, 6, 7, and 9. Similarly vacuoles or fat or both were noted in all the lutein cases except 1, 3, 4, and 6; fat was demonstrated in Cases 2, 5, 8, and 9; in Case 7 "the cells were either granular, or translucent, or vesicular, and fat could not be demonstrated with osmic acid"—but there is no information regarding the fixative. (Compare Figs. 5 and 6.) Nevertheless the cytoplasm was apparently not as a rule quite as clear or as extensively vacuolated in the lutein tumours as in the hypernephromas.

(*b*) Capillaries, or thin-walled blood-vessels, were noted as a feature of both tumours except hypernephroma Case 4 and lutein Case 7; the tumour cells usually lay directly upon them. In hypernephroma Case 3 they formed "cell mantles," in lutein Case 9 they were arranged "radially," and in lutein Case 1 like a "perithelioma."

(*c*) Fibrous tissue stroma varied in amount in both groups of cases.

(*d*) Glycogen was mentioned as present in hypernephroma Cases 1, 2, 3, 6, and 9, but *not* in the lutein growths.

(*e*) Gland-like lumina were mentioned as present in hypernephroma Cases 1, 3, 5 and 9—they were probably present in Cases 2 and 6—but they are *not* mentioned in the lutein growths.

Apart from the absence of vacuolation, etc., or of fat in the cytoplasm of some of the lutein tumours, it might be imagined that a *real* difference had at last been discovered between the two types of growth, but this is improbable for the following reasons:—

Glycogen was first demonstrated in ovarian "hypernephroma" by Peham (1899), who regarded its presence as *evidence of their suprarenal origin,* because he says "Lubarsch (1895) had found glycogen in hypernephromas of the kidney, and certain other tumours, but in ordinary ovarian tumours glycogen was practically absent." Three other authors describing ovarian hypernephromas adopted Peham's view. But subsequent investigations showed that glycogen was not specially characteristic of hypernephromas. Thus Lubarsch (1905), examining 1,544 tumours, found it in 50.7 per cent. of sarcomas, and 43.6 per cent. of cancers, though not in 10 cancers

of the ovary, while Behr, quoted by Gierke (1905), also observed it in almost all sarcomas—provided they were examined early enough. Gierke found glycogen constant and abundant in "endotheliomas."

Lubarsch (1905) concluded that four factors appeared to determine the occurrence of glycogen, viz., (1) The origin from embryonal tissues. (2) The origin from cells normally containing glycogen. (3) The absence of mucoid and colloid degeneration, and the frequent presence of fatty change (Gierke also found that fatty changes and glycogenic infiltration were determined by the same conditions, and Best, according to Ewing, noted that secondary deposits of glycogen occurred in necrotic tissues). (4) The presence of numerous delicate blood vessels in the tumour stroma and their intimate connection with the parenchyma as in angio-sarcoma and endothelioma. Factors 3 or 4, and perhaps 1, explain the occurrence of glycogen in the hypernephromas.

There is no evidence on the other hand that the authors looked for glycogen in the lutein growths. Had they done so I am convinced they would have found it in some, perhaps all; for although Gierke failed to demonstrate this substance in either the follicles or the corpus luteum of different human ovaries, yet factors 3 or 4, and perhaps 1, were present in the lutein tumours.

Lumina. It has already been pointed out here how pathologists, misled by Grawitz, have specially sought for gland lumina or well formed pseudo-lumina in supposed "hypernephromas" of the ovary, etc., whereas in reality even ill-formed pseudo-lumina are *very* rare in hypernephromas of the suprarenal gland itself.

Therefore the frequent presence of pseudo-lumina in the ovarian "hypernephroma" has no significance; it is explained possibly by artefact but most probably by regressive changes. It is very suggestive that in addition to lumina, small degeneration cysts were described in Cases 1, 3, and 9; in Case 9 lumina were *only* present in the peripheral part of the tumour which *contained cysts;* in Case 5 it was noted that one of the tubules contained "loose cellular elements." Lumina were undoubtedly present in some of the lutein tumours, for degeneration cysts were mentioned in 4 cases, in Cases 2 and 6 they were lined by tumour cells. Obviously cysts of microscopical size, perhaps in process of formation, would resemble lumina.

The striking omission to mention the presence or absence of glycogen or lumina in the lutein tumours is explained very simply. *Only one of the sixteen authors describing the nineteen ovarian tumours ever discusses whether what he named a lutein growth might be a hypernephroma, or* vice versa. The exception was hypernephroma Case 5A, where Professors Laguesse and Curtis after

considerable difficulty decided their growth was "very probably" a hypernephroma, and not a lutein tumour.

The decision as to which group the tumours belonged was mainly due to *personal bias;* though present or repeated past pregnancies, or the absence of clear or very vacuolated cytoplasm may sometimes have been regarded as evidence of lutein origin. But when once the author decided his specimen was a lutein tumour, he did not trouble to look for glycogen, or allude to the presence or absence of lumina.

Conclusion. The impartial critic, considering the clinical history and the macroscopic and microscopic characters of the two groups of tumours, and making due allowance for personal equation of the various authors describing them, is forced to the conclusion that the great majority if not all are of the same type, and of *lutein origin.* In some of the "hypernephromas" the cell cytoplasm has for unascertained reasons undergone an unusual amount of fatty or "hyaline" degeneration which is so common in lutein cells. (Allbutt, Playfair and Eden, 1906.) The difficulty that some of the "lutein" tumours occurred long after the menopause, was first noted by Rokitansky. Grouzdew suggested that the tumour in his patient aged 60 "arose from the cells enveloping the corpus albicantium." In that case they would be derived from the interstitial cells which have taken on some lutein characters.[1]

3. Clinical.

Absence of changes in sex characters, i.e., of "suprarenal virilism" with ovarian "hypernephroma."

Since Bulloch and Sequeira's classical paper in 1905, our knowledge of the association between suprarenal cortical tumours and secondary sex characters has greatly advanced; it may be summed up as follows:—

1. *Congenital lesions.* Equal bilateral cortical hyperplasia or occasionally large accessory suprarenals, are often associated with pseudo-hermaphroditism. This association was noted in 15 per cent. of female pseudo-hermaphrodites, *i.e.* females approximating the male type, but only 0·7 per cent. of male pseudo-hermaphrodites. In the former hirsutes of the male type was also present and often male physique. Thirteen cases have been recorded, 12 females, 1 male—doubtful, see later—(Glynn, 1912).

1. Goodall (1920) described the ovary of a rabbit just after parturition in which "every interstitial cell seems to have been converted into cells resembling, in every particular but one, the true lutein cells of the corpora lutea. That one and only distinction consists in a slightly smaller size of the extra-corpus cells."

2. *Acquired lesions.* Unilateral primary cortical neoplasm, *i.e.*, suprarenal hypernephroma, usually malignant, produces changes in secondary sex characters.[1]

(*a*) In girls, apparently invariably.[2] These are precocious growth, hirsutes usually of the male type,[3] often obesity, often hypertrophy of the external genitals, particularly of the clitoris,[4] two girls had a deep voice, one girl of 11 menstruated (see later). Seventeen cases, verified by post-mortem, have been recorded, ages 1—11, usually 3—7 (Glynn, Lit. 1912, also Jump, 1914, Hijmans, 1915, Turnbull, 1920).[5 6]

(*b*) In boys, apparently invariably. These are precocious growth, hirsutes of the male type, either obesity or great muscular development, precocious development of the external genitals, but apparently no potency (see later). Four cases, verified by post-mortem, have been recorded, ages 4—16 (Glynn, Lit. 1912, also Baldwin, 1914).

(*c*) In women before the menopause, in at least half the cases (Glynn 1912). These are hirsutes of the male type, almost invariably amenorrhœa with atrophy of the uterus and ovaries (see later), often atrophy or non-development of the breasts, occasionally deepening of the voice, rarely psychoses; obesity is sometimes present in the early stages. Eight, perhaps nine, cases, verified by post-mortem, have been recorded[7] (Glynn, Lit. 1912, also Hewetson and Glynn 1913, Launois Pinard and Gallais 1911, Guemes 1917,

1. The common primary neoplasm of the *medulla* is the "neuroblastoma" or "glio-sarcoma," formerly called "round-celled sarcoma." (See Dunn, lit. *Journ. Pathol. and Bacteriol.*, 1914-15, vol. xix, p. 456). Neuroblastomas most frequently occur in young male children; metastases are numerous; they sometimes develop on the skull, and may produce exophthalmos (Hutchinson's type). These tumours do *not* cause changes in sex characters.

2. Bruchanow (*Zeitsch. f. Heilkunde*, xx, 39) described a *medullary* carcinoma in the right adrenal of a girl of 14 months which also involved the kidney hilum. There is no mention of abnormal development of the child, and no clinical history was available.

3. Viz., on the *face*, limbs, chest and back and also linea alba, *i.e.* between the umbilicus and pubes.

4. Hypertrophy of the external genitals was noted in the cases of Ritchie, French, and Fox, and hypertrophy of the clitoris in the cases of Orth and Miller (see Glynn), also Turnbull, Hijmans and Jump.

5. There is sometimes increased pigmentation, as in Ogle's and Fox's cases, but no true bronzing of the Addisonian type (see Bulloch and Sequeira).

6. Guinon and Bijon describes a case which was still alive (Guinon et Bijon, *Bull. de la Soc. de pediat. de Paris*, Mars. 1906, p. 129). Phillips-Lambright (*Arch. of Pediatrics*, May 1920, vol. xxxvii, No. 5, p. 282) also describes premature sexual development in a girl aged 7, still living, in which the "cortical portion of the adrenal is most likely to be at fault." The child probably has an *ovarian tumour*.

7. One of these cases, Ogston's, III, is not typical (see page 47).

Fraser 1916—doubtful case, see page 49). Hewetson's striking case is quoted as the type—see Appendix, Case 2.

A woman who had always been healthy, ceased to menstruate at the age of 28. Soon after cessation she grew stouter and hair appeared on the face, chest and abdomen. At 30 her voice became deeper and harsher. At 40 the chin, neck and upper lip were covered with strong hair for which she shaved regularly, and the breasts flattened to the masculine type. At 44 a tumour, weighing 12 lbs., was removed from above the left kidney, microscopically a true suprarenal hypernephroma. The patient died from shock. The post mortem revealed an atrophied uterus and small fibrotic ovaries.

(*d*) In women after the menopause, no changes, or at any rate, no striking changes occur. Seven cases have been recorded, three by Ramsay and four by Woolley (Glynn 1912).

Slight changes, such as a moustache or deepening of the voice, might not be thought worthy of record. I have met one such case *associated* with cortical hyperplasia :—

R. A. G., aged 55, died from emphysema and bronchitis with tricuspid regurgitation in the Liverpool Royal Infirmary. She weighed 16 stone; there was marked growth of black hair on the upper lip and over the chin, the average length of the hairs being half an inch. The adrenal glands were moderately enlarged, their surface was locally irregular, due to cortical adenomata, verified microscopically; the largest was 1·4 cm., and the smallest 1 mm.; they weighed 8 grammes each.[1]

(*e*) In men, though suprarenal cortical tumours are frequent (11 cases described by Woolley, ages 40 to 73; one by Davies aged 25; one by Lasagna aged 61), only a single doubtful case has been recorded, Bittorf's (1919); here the changes in sex characters approached the *female* type.

A man, aged 26, not unduly obese, had noticed enlargement of the breasts for seven months followed by decline in sexual potency, and within the last month by the appearance of a tumour in the left flank. The testicles were very small. The hair on the body and face was of the male type. The voice was high but not higher than normal. *X*-rays showed there was nothing abnormal in the sella turcica and the sight was unaffected. There were slight pigmentation of the face and rise of blood-pressure. Death was preceded by metastases in the liver and progressive cachexia. Only six lines are devoted to the post mortem report of this unique case. There was a large hypernephroma of the left suprarenal, cortical

1. The normal weight in women 50 to 60 is given as 4·8 to 7·2 grammes, Krause, Daten u Tabellen, Vierordt, Fischer, Jena 1906, p. 43; and 9·4 grammes, Scheel, *Virchow's Arch.* 1908, 192, p. 507.

type, compressing the left kidney; "the clinical diagnosis was confirmed in every particular." It is unfortunate that there is no reference to the macroscopic and microscopic appearances of the pituitary; for the case may have been after all dystrophia adiposo-genitalis, and the hypernephroma a coincidence. On the other hand gynæcomastia sometimes follows atrophy of the testicle secondary to inflammation; Halban reports a case apparently following orchitis from mumps.

Meixner's quite unique case of *male* pseudo-hermaphroditism in an infant with three small accessory suprarenals near the testicles, may perhaps be compared with Bittorf's. But both suprarenals were of normal size, so that the net increase of cortical tissue is less than any of the female pseudo-hermaphrodites; apart from this the presence of the accessory suprarenals may be a mere coincidence, for they are very common in infants.

The division between congenital bilateral hyperplasia of the suprarenal cortex associated with pseudo-hermaphroditism and acquired unilateral neoplasm producing changes in the secondary sex characters, is not absolute; certain cases of the latter appear to be connecting links with the former. First, with neoplasm there is often clitoris hypertrophy, as already mentioned. Secondly, in three cases of neoplasm *both* suprarenals were enlarged, though in two unequally, viz., in Bortz and Thummin's case of a woman, aged 17, her left suprarenal was "as big as a fist," while her right contained "two nodular tumours the size of cherries"; and in Richard's case of a girl of 8, growth in the left kidney was as big as a cocoanut, and in the right about half the size. The third case, Ogston's, is the best connecting link.

M. C., a girl aged 16, apparently in good health, was found dead in bed. She had never menstruated. There is no mention of hirsutes. At the post mortem neither the breasts nor the pelvis were developed. The ovaries were exceedingly small and both full of small cysts; the uterus was not bigger than that of a new-born child. Both suprarenals were enlarged to half the size of the kidney. The cause of death was not discovered.

Nomenclature. Cases of abnormal sex characters with suprarenal cortical neoplasms are so frequent that Lucien and Parisot (1913) suggest the term "syndrome cortico ou interrèno-gènital," this, however, is not descriptive. Gallais (1914) calls it "virilism," which is defined in the Oxford English Dictionary (1917) as a "form of hermaphroditism."

The best term is "suprarenal virilism"—the addition of the word "cortical" is cumbersome. Suprarenal "virilescence" is inapplicable. Virilescence is defined as "the acquiring of characters more or less like those of the male, often observed in barren or old

females" (Webster's Dictionary, 1911), but suprarenal virilism developes in the young or middle-aged.

In *women* the term "suprarenal virilism" certainly describes the usual clinical picture of the disease. In *girls* it is less descriptive, for male type of hirsutes is not always present, though some cases with female hirsutes have other characters suggesting "maleness" as clitoris hypertrophy or even a low-pitched voice or both (Hijman's patient). The term also distinguishes the disease from true precocious development with menstruation—sometimes associated with ovarian tumour. In *boys* the term is descriptive for male hirsutes is invariably present—and the fact that the testicles are apparently always undeveloped suggests "form of hermaphroditism" as required by the definition. The term also distinguishes the disease from precocity, occasionally true precocity, sometimes associated with tumours of the testicle or pineal gland. The term "suprarenal *precocity*" in a boy or girl conveys the idea of abnormal growth, but not of the assumption of certain sex characters of the male type, besides it is not uniform with the term "virilism" as applied to women.[1]

Amenorrhœa, after hirsutes, is the most constant striking symptom of hypernephroma in ***women***. An analysis of the eight

1. Gallais describes two clinical types of disease produced by suprarenal cortical neoplasm, which are quite unnecessary.

1. *The menstrual type* (dysmenorrhée, amenorrhée complète, hypertrichose, adiposité, p. 137) occurring in women. Five examples are given:

(*a*) Marchand's case of a girl aged 20 with a suprarenal cortical tumour, who suffered from irregular menstruation, Observation XLV. I included this among suprarenal hypernephroma in women "without changes in sex characters" (1912).

(*b*) Davis's case of the epileptic woman, Observation XLVI, described elsewhere by him as Observation XL under virilism! I included this among "suprarenal virilism" in women.

(*c*) Goldschwend's case of a woman with hirsutes and amenorrhœa, Observation XLVII. I included this among "suprarenal virilism" in women.

(*d*) Santi's case of a woman with hypernephroma of the ovary and kidney who had metrorrhagia, Observation XLVIII. It has already been pointed out this is not a true hypernephroma.

(*e*) Dumout, Cailliau et Carianopol's case of a very obese woman with a suprarenal adenoma the size of a hen's egg, but her age and menstrual history is not given!

2. *Obstetrical type.* "In this the suprarenal tumour coincides with development of tubal pregnancy." Two examples are given:

(*a*) Lecene's case of a woman with a ruptured tubal pregnancy, who had an accessory suprarenal in the left broad ligament the *size of a millet seed*! viz. Observation L, which has been included in the Embryological part of this paper.

(*b*) His own case of a woman with tubal pregnancy who died suddenly after injection of iodine into the uterus and was found to have an adenoma of the suprarenal, the size of a pigeon's egg. Gallais also quotes three doubtful cases of the obstetrical form—doubtful because there was no post mortem.

cases in women before the menopause reveals the following: in five complete cessation is mentioned, viz., Glynn and Hewetson's for 16 years before death; Goldschwend for 3 years, Guemes for 3 years, Bortz for 2 years, Pinard for 1 year before death; in Davis' case the date is not given. Menstruation had almost certainly ceased in Winkler's (Case 7), because the uterus was very small, and in Ogston's because the uterus was the size of a small child's. In Thornton's patient the hirsutes and tumour appeared "soon after öophorectomy." In another case (Bovin's) a large suprarenal cortical tumour in the *broad ligament* produced striking changes in sex characters, including complete amenorrhœa; but *menstruation reappeared two months after its removal* (see page 50).

The hirsutes always developed simultaneously with or shortly after the amenorrhœa.

Fraser (1916) has described a possible exception to this rule about amenorrhœa.

A woman, aged 28, six feet high, of excellently developed musculature, had a thick growth of coarse black hair on the chest, arms and legs, and a small moustache. The mammæ were undeveloped and the chest decidedly of the male type. Menstruation was regular. At a laparotomy an encapsulated tumour was removed from a false pelvis. It apparently arose from the lower pole of the kidney with which it was "intimately united." Microscopically the growth was "very similar" to that described by "Bulloch and Sequeira," being adenomatous rather than carcinomatous, "there were no papillary, cystic or tubular formations." The patient died shortly afterwards from pericarditis. The left adrenal could not be found at the post mortem; there were no metastases. The author believed the "tumour originated from an accessory adrenal in the capsule of the kidney, otherwise it was a hypernephroma of a misplaced adrenal."

It is not certain that this tumour was derived from suprarenal tissue because: (1) The position of the tumour was unusual; when the case came to be described the "macroscopic specimen could not be found"! Though the author clearly demonstrates that it was microscopically unlike the renal "hypernephroma," the histological description is incomplete and the pictures unconvincing. (2) There is no information as to the patient's age when the hirsutes developed, besides the growth on the face was slight. It is well known that a masculine physique may be due to other causes than adrenal tumours, viz., some pituitary lesions or ovarian insufficiency (Blair Bell).

In *children*, however, one case of menstruation has been recorded with suprarenal cortical tumour, viz., Bulloch's (1905).

The patient, a girl of 11, was normal up to the age of 10, when,

coincident with the appearance of the suprarenal tumour, she "showed precocious development as manifested in her size and bulk, the *onset of menstruation*,[1] the development of hair on the pubes and face, and the maturity of the mammary glands."

This case is an exception to the general rule, in fact it is apparently unique, for none of the other 16 girls with suprarenal virilism, *menstruated*. It must be admitted, however, that these girls were younger than Bulloch's patient, viz., $8\frac{1}{2}$ years one case, 7 years three cases, the rest 5 years or less.

Still many instances of menstruation in early childhood, even just after birth, are recorded. Roger Williams (1902) collected 60 cases occurring up to the age of 7 due to no obvious cause, and a few others associated with ovarian tumours. Further, he states that at later periods "so many examples have been reported that it seems unnecessary to cite individual cases."

In *males* the effect of suprarenal tumours on the testes has some bearing upon the effect on the ovary, *i.e.*, on menstruation. The evidence is inconclusive. In Emery's case a boy, aged $4\frac{3}{4}$, they were "not unduly developed," and microscopical sections revealed no spermatozoa; in Adams', a boy of 16, there is no information; in Baldwin's, a boy of 6, "the external genitals were those of a man except that the testes were small and incompletely descended"; in Linser's, a boy of 5, the testes were the size of pigeon's eggs, but there is no information concerning the presence of spermatozoa.

In Bittorf's doubtful case in a man, there was a decline of potency and the testicles were very small.

Absence of "suprarenal virilism" with ovarian "hypernephroma."

Seven out of the ten patients with ovarian tumours had not reached, or at least had not passed the menopause, the ages being under 45 ? (Case 1), 18, 40, 4, 27, 27, and 51 (Case 9).[2] They were therefore not too old to develop suprarenal virilism. Hewetson's patient was 36, Guemes' about 35, when these developed, and Thornton's was 36 when her beard fell out after removal of hypernephroma.[3]

1. There are no particulars except that she had menstruated for 15 months. At the post mortem "the uterus was much larger than normal, the cervix and the body being of equal length, *which indicated a much greater hypertrophy in the cervix than in the corpus*. (Italics mine.) The ovaries were equal in size, and perhaps a little larger than normal. On section several corpora lutea were found, one being of recent date" (Bulloch and Sequeira).

2. The clinical data of some of the cases are lacking.

3 Before this operation her face and body were covered with "long silky hair" which she shaved. Seven months after the operation she wrote to her doctor, Dr. Myrtle: "I am much like my old self and have all the external appearances of other women."

Yet no changes were noted; hirsutes were absent in all except Case 5 (see later), and permanent amenorrhœa is only mentioned in Cases 4 and 10, in the former cessation was probably due to emaciation brought about by the disseminated growths from which the patient died six months later.

Further, assuming for the sake of argument that the lutein tumours were hypernephromas—as the authors who described the ovarian "hypernephromas" would certainly have called some of them—we find that nine of the patients had not yet passed the menopause, their ages being 30, 32, 24, 38, 21, 45 and 48; in Wendeler and Martin's cases the exact age is not given. Yet not one developed suprarenal virilism.

It may, however, be suggested that ovarian "hypernephroma" (Gaudier's Case 5A) in a girl aged 4 with "breasts and external genitals of an adult," who had menorrhagia and metrorrhagia, was really a suprarenal hypernephroma, from its resemblance to Bulloch's case of suprarenal tumour already alluded to. This is improbable, however, because menstruation occurred in only one out of the 17 girls with these tumours; secondly, there was no growth of the hair on the face, recorded in 9 out of the 17 cases; and lastly no hypertrophy of the clitoris or external genitals, recorded in 8 cases.

It will be remembered also that Laguesse only decided against Gaudier's tumour being a lutein formation after great difficulty. Roger Williams mentions 55 cases of precocious menstruation in girls between birth and 5 years of age, due to no obvious cause; he also states that "mature Graafian follicles, corpora lutea and recent ovarian cicatrices" have been discovered even in the ovaries of newly-born infants. The weight of evidence therefore indicates that the tumour was of lutein origin.

Objections to the clinical argument.

1. *Renal Hypernephroma.* These are very common tumours. Garceau collected 176 cases from the literature; while Ellis referred to 163, viz. 157 in the kidney, 2 in the liver, 1 in the uterus, and 3 in the suprarenal; and Zehbe to 37 in the kidney and 1 in the suprarenal. Now it may be objected that as suprarenal virilism rarely if ever occurs with these common tumours, there is no reason why it should occur with the uncommon ovarian "hypernephromas." As a matter of fact there are only two, perhaps three, cases on record of suprarenal virilism being due to a hypernephroma, which may possibly have originated in the kidney but probably did not.

The three cases are: (1) Richards, a girl aged 8½, both kidneys were involved—which is unlike a primary renal tumour—and there

is no mention of the microscopical structure, or of the suprarenals! (2) Jump (1914), a girl aged 7, with typical suprarenal virilism including a bass voice; the growth involved the whole of the right kidney, and there was no line of separation from the suprarenal, so it may have originated in the suprarenal; there is no microscopical description of the tumour. (3) Fraser's doubtful case in a woman of 28 has already been referred to.

But, as already pointed out, many modern pathologists are convinced for developmental, histological and other reasons, that the renal hypernephroma is rarely derived from the suprarenal cortex. Further hypernephromas are comparatively rare in children, and women before the menopause, first because they are commoner in males than in females in the proportion of 102 to 71 (Garceau), second, because only two per cent. occurred in both sexes from 1 to 20 years of age, sixteen per cent. from 20 to 40, and twenty-nine per cent. from 40 to 50.

Hence the absence of suprarenal virilism with these renal tumours is really a most striking corroboration of the clinical argument.

2. *Ovarian tumours* have been described which were associated with change in sex characters by Apert and Pozzi respectively. Consequently it may be objected that the clinical argument is invalid. Investigation, however, proves this is not so.

(*a*) *Apert's group* (1910). Here the changes were typical of suprarenal virilism, viz., hirsutes, cessation of menstruation, clitoris hypertrophy, etc. But Apert's tumours were not called hypernephromas, for they were of the *usual cystic type*. He quotes three cases, all of which are badly reported: (1) Alberti (1906), "a normally built girl, in whom menstruation was regular from 16 to 19, completely ceased menstruating at 20. Simultaneously the body became covered with hair, a beard grew, the breasts, previously well developed, atrophied, the muscles, especially the deltoids and pectorals, hypertrophied, the voice became deeper, and the clitoris enlarged. At the age of 23 she died from a twisted right ovarian tumour which was discovered shortly before death. The tumour was the size of a man's head, and proved microscopically to be a "*simple cystoma-multiloc. pseudo-mucinosum* hæmorrhagically infiltrated." Some of the cysts contained epithelium mixed with the blood, but there was no epithelium upon the cyst walls. Only the uterus and left ovary were examined at a partial post mortem, the latter was said to be normal. (2) Duradonna, the symptoms began at 24. A pedunculated serous cyst of the right ovary was removed! (3) Audain (1893). The patient was a mulatto woman aged 49. Two dermoids of the usual microscopical

appearances and a parovarian cyst were removed; the latter was so typical that it was not examined microscopically! (4) Roten (1895), quoted by Scheuer. A girl of 17, who had menstruated normally for three years, suddenly developed amenorrhœa and a high degree of hypertrichosis all over the body "as the result of a double ovarian polycystoma."

There is no evidence that the suprarenals were examined in any of these four cases; in fact the association between hirsutes, etc., and tumours of these organs was probably unknown to the writers, for they were reported many years ago.

Furthermore, if these ovarian tumours really caused the hirsutes one would have expected a record of a partial or complete recovery after the operation, in some of the patients. Knowsley Thornton's case of a woman, whose hirsutes disappeared after the removal of the suprarenal tumour, has already been referred to. Clement Lucas' patient, a girl aged 7, menstruated several times, the mammæ were well developed, pubic hair was present; but after the removal of a solid ovarian tumour most resembling a round-celled sarcoma with alveoli, menstruation ceased and the signs of puberty gradually disappeared (see Guthrie and Emery). Sacchi's patient, a boy aged $9\frac{1}{2}$, showed premature development; a large tumour of the right testicle containing an "epithelial growth" was removed, the boy then became more child-like and his beard fell out (see Guthrie and Emery).

McAuliff (1916) described a case somewhat resembling Apert's. A woman, aged 63, was diagnosed to have an ovarian tumour when about 23. She grew a moustache, and four years later a beard which she used to shave. A pedunculated cystic tumour of the right ovary was removed forty years later by laparotomy, which, as it contained ciliated columnar epithelium and greyish hair, was called a dermoid cyst. It is not stated whether there was a premature menopause. "The patient's daughter at the age of 43 had an increased growth of hair on the upper lip for thirteen years."

(*b*) *Pozzi's Group* (1911). Here the changes were less typical of suprarenal virilism, viz., slight hirsutes or amenorrhœa, or both, with perhaps a male voice. But the ovarian tumours were solid or semi-solid. Pozzi alludes to four cases; a solid ovarian tumour in a woman of 30 (his own case), another in a woman of 21 (Fehling's case), both were microscopically a sarcoma-globo-cellulaire; also to semi-cystic ovarian tumours, microscopically teratomatas, in a woman of 29 (Friedman's case), and a woman of 16 (Litten's case). But these changes were not *caused* by the ovarian tumour, for all the patients were female pseudo-hermaphrodites, and the clinical history demonstrates that the tumours apparently developed a short time before removal.

"Hypernephroma" of the testicle.

There is no *a priori* reason why, if hypernephromas of the ovary occur, they should not also occur in the testicle. I have discovered no records of any *in* this organ.[1] Debarnardi (1907), however, has described a congenital hypernephroma in the immediate neighbourhood of the testicle which was removed ten months after birth. It measured $7\frac{1}{2}$ by 5 centimetres, and was connected to the upper pole of the testicle, by the epididymis, but the testicle itself and its rete were intact. The colour of the tumour is not mentioned. There was a small centre resembling the zona fasciculata, while the rest was a sarcoma of round, spindle, and giant cells: at one place the two types of growth merge together. Glycogen was present, but neither cysts nor lumina.

There is no lutein tissue in the testicle which might grow into a "hypernephroma"; therefore the fact that hypernephromas of this organ apparently do not occur is strong evidence against their occurrence in the ovary. The extraordinary similarity in the development of the ovary and testicle recently emphasized by Goodall strengthens the force of this argument.

"Hypernephroma" of the broad ligament apparently not originating in the ovary.

Case 1. Weiss (1898, No. 2). A girl, aged 17, unmarried, complained of menstrual irregularity and abdominal pain. A tumour, the size of a man's head, was found in the right broad ligament, which was incompletely enucleated. Macroscopically it was red-white and butter-yellow, with a marked tendency to hæmorrhage and necrosis; the ovary formed a prominence on the superior surface but was separated by fibrous tissue. A minute "cortical rest," verified microscopically, was found in the broad ligament quite independent of the tumour. Microscopically it was composed of large polygonal cells with vesicular nuclei and scanty cytoplasm, other cells showed marked fatty infiltration. They were arranged in an irregular network around capillaries, often forming "cell mantles," or in a gland-like manner around spaces containing hyaline material. Glycogen was present. The diagnosis of hypernephroma was made partly on account of the presence of glycogen, fat, cell mantles, and lumina; but the author admits the appearances are unusual. (See Fig. 10.)

Case 2. Eastwood (1902). A woman, aged 48, who had not menstruated for eight years, complained of abdominal pain and a dark brown discharge for fifteen months. A solid encapsulated tumour, $17\frac{1}{2} \times 11\frac{1}{2} \times 5$cm. was found in the right broad ligament near to but separate from the uterus; it contained a cyst with two pints of yellow fluid. The ovaries were normal. Macroscopically the growth was yellow with streaks of hæmorrhage and some necrosis. Microscopically it was composed of large poly-

1. Ewing (p. 742) alludes to a hypernephroma of the testicle described by Chevassu, but I can find no record of such a tumour in Chevassu's paper, "Tumeurs du Testicule," Steinheil, Paris, 1906.

hedral cells with " granular and vacuolated protoplasm " embedded in a vascular stroma, parts had a striking resemblance to zona glomerulosa. In places there was a tubular appearance. Fat was present in irregular distribution. (See Fig. 12.) The patient was well 19 months after operation.

The histology is very carefully studied and the author, after deciding that the growth was not derived from the Wolffian body or duct and not a " mixed " tumour, concludes it was of suprarenal origin.

Case 3. Alamartine (1912). A woman, aged 56, complained of severe metrorrhagia, emaciation and œdema of the legs; a tumour, the size of an orange, was removed from the base of the left broad ligament, it was invading the bladder, ovary and tube. Macroscopically it was locally lobulated, sulphur-yellow with reddish areas due to extensive vascularisation and hæmorrhage. Small cysts filled with white substance coloured with blood were also present. There were secondary nodules in the right ovary. Microscopically it was composed of two types of cells, lying in irregular groups in a stroma of connective tissue and embryonic vessels; they often had a perivascular arrangement. Some cells were large polyhedral with absolutely clear cytoplasm due to the presence of fat, like "the spongiocytes of the adrenal cortex." They occasionally contained two nuclei. Others were small with relatively large nuclei and dark staining cytoplasm; there were also intermediate cells (see Fig. 11). The author thought the tumour arose in the broad ligament from an aberrant suprarenal. The patient died the day of the operation from hæmorrhage and shock. There was no post mortem.

These broad ligament tumours are probably not true hypernephromas.

Although it must be admitted that the embryological evidence supports an accessory suprarenal origin, the histological and clinical evidence points in the opposite direction.

Histological. Weiss' tumour, as the author says, has an unusual appearance; Eastwood regarded it as an " angio-sarcoma commencing about the ovarian hilum." Alamartine's resembles many of the hypernephromas and lutein tumours of the ovary; the " spongiocytes " described in it were also noted by Massabuau in his lutein growth (Case 9B). Eastwood's is the only tumour at all resembling a true hypernephroma.

Clinical. Weiss' patient was only 17, but there is no mention of suprarenal virilism. Eastwood's patient, aged 48, had not menstruated for eight years; if, however, the amenorrhœa was due to a true hypernephroma hirsutes would probably develop, for Goldschwend's patient was 36 when this occurred. Alamartine's patient, aged 56, was too old for striking changes in sex characters.

Summary. In my opinion the cases of Weiss and Alamartine were not hypernephroma, but Eastwood's may have been. If these tumours are not hypernephromas, what was their origin? It is possible that they arose from the ovary after all, or perhaps from some unusual embryonic remnant in the broad ligament: Alamartine's tumour may be a metastasis, for there was no post mortem.

A probable case of true hypernephroma of the broad ligament producing suprarenal virilism.

If a hypernephroma should develop from an accessory suprarenal in the broad ligament of a young woman, one would expect changes in sex characters. Bovin (1910) has published a striking case of this nature.

A woman gradually ceased menstruation in her nineteenth year, after the birth of her second child. With complete cessation she grew a beard, and much hair on the abdomen. The breasts and external genitals were normal. At 28 a large tumour adjacent to the left ovary was removed; the right ovary and uterus were atrophied. Two months later menstruation recommenced, and continued regularly; but the beard persisted.

Macroscopically the tumour was indistinctly lobulated, it measured 8 by 5 by 8 cm., the surface was smooth, white and fibrous, the substance soft and *yellow*. On the internal part of the tumour there was a nodule the size of a nut which was distinguished by its grey-red colour and numerous vessels; on microscopical examination this proved to be an atrophied ovary. The tumour itself was composed of epitheloid cells, arranged in an irregular meshwork of capillaries. The majority of the cells were large and polyhedral of a diameter 30 to 35 μ with finely granular cytoplasm containing large vacuoles with fat, also big nuclei rich in chromatin and with a single nucleolus; a few of the cells, probably younger, were smaller and less vacuolated. There were necrotic and also hæmorrhagic areas with blood pigment. The general characters of the tumour were said to recall those of the suprarenal capsule; on account of the position of the ovary, it was regarded as of parovarian origin.

It must be admitted that the microscopical description of the tumour, which is not illustrated, does not *clearly* differentiate it from the ovarian "hypernephromas" and lutein tumours. Nevertheless the large size of most of the cells, their big nuclei rich in chromatin, and the presence of smaller cells, both of which only contain vacuoles and not clear cytoplasm, is very suggestive.

Apart from this the evidence is conclusive that the tumour is a true hypernephroma of an accessory suprarenal. It is all the more remarkable because only four "hypernephromas" have been recorded in the broad ligament, although accessory suprarenals are relatively common there.

General Summary and Conclusions.

1. Certain solid yellow tumours of the ovary have been called "hypernephromas." This was partly on the assumption that suprarenal cortical tissue is common in the ovary, and partly on

account of their yellow colour, and partly perhaps from the presence of fat, glycogen or lumina; but particularly on account of the general resemblance of the groups of clear or very vacuolated cells lying in a capillary stroma, to the zona fasciculata of the suprarenal cortex.

2. It is now generally recognized that the smaller tumours, clinically unimportant, are lutein formations; but the larger tumours, clinically important, and structurally less like the corpus luteum, are still regarded as "hypernephromas." Ten such large tumours have been described, including two in the broad ligament, apparently originating in the ovary; they are usually malignant, and usually contain hæmorrhagic and necrotic areas and sometimes degeneration cysts.

3. Nevertheless it is quite unproven that these large tumours are "hypernephromas" for the following reasons:—

A.—*Embryological.* Contrary to the general belief there is no proved case of accessory suprarenal *in* the ovary. Sixteen observers have recorded 34 cases of these bodies in the broad ligament or its vicinity, but only *once* where they were close to the ovary. Three observers have recorded five alleged accessory suprarenals *in* the ovary of *women*, but they were almost certainly lutein formations on account of the presence of cysts or fibrin. Though accessory suprarenals are relatively much commoner in the very young than adults yet only one doubtful case is recorded *in* the ovary of an *infant*.

Many observers have recorded accessory suprarenals in the vicinity of the testicle, though they are exceedingly rare in the corpus Highmor: yet only one doubtful case is recorded *in* the testicle. This corroborates the experience with regard to the ovary.

B. *Histological.* The ovarian "hypernephroma" is quite unlike the true suprarenal hypernephroma, *i.e.*, the primary neoplasm of the cortex of the suprarenal gland. The latter is distinguished by much greater variation in the shape and size of its cells and their nuclei, by the absence of the characteristic clear or very vacuolated cytoplasm, and apparently by the complete absence of well-formed gland-like lumina.

Whereas the resemblance of the ovarian "hypernephroma" to the suprarenal cortex is more or less close, the resemblance of the suprarenal hypernephroma to the cortex is usually so slight, that none but an expert would suspect its origin.

C. *Clinical.* Suprarenal hypernephroma produces striking changes in sex characters: (i) Apparently invariably in girls (17 cases recorded), notably precocious growth, hirsutes—usually of the male type, sometimes obesity, sometimes clitoris hypertrophy, etc.

(ii) Apparently invariably in boys (4 cases recorded), notably precocious growth and hirsutes of the male type, etc. (iii) In at least half the cases of women before the menopause (8, perhaps 9, cases recorded), notably hirsutes of the male type, amenorrhœa, atrophy of the uterus and ovaries, often atrophy or non-development of the breasts, sometimes deepening of the voice, sometimes obesity, rarely psychoses. (iv) In woman after the menopause no sex changes, or, at any rate, no striking changes occur. (v) In men sex changes apparently never occur. The term "suprarenal virilism" best describes these acquired changes in sex characters.

Suprarenal virilism was absent in the seven patients with ovarian "hypernephroma" who had not passed the menopause; one, however, a girl aged 4, menstruated, but the hirsutes was of the female type, there was no clitoris hypertrophy, and the histologists had great difficulty in deciding it was *not* a lutein tumour.

Objections. (i) The absence of suprarenal virilism with renal "hypernephroma" does not invalidate the clinical argument, because these tumours are rare in children, and women before the menopause; besides the great majority are not derived from suprarenal cortical tissue. (ii) Five cases of ovarian tumour clinically typical of suprarenal virilism have been recorded (Apert's syndrome). But these tumours were not called "hypernephromas," for they were cystic or dermoids; further there is no evidence that they produced the sex changes or that the suprarenals were even examined. (iii) Four cases of solid or semi-solid ovarian tumours clinically somewhat resembling suprarenal virilism, have been recorded (Pozzi). But these tumours were not called "hypernephromas"; they all occurred in female pseudo-hermaphrodites, and they apparently only developed a short time before removal.

4. No case of hypernephroma of the testis has yet been recorded. This corroborates the conclusion that *the existence of "hypernephroma" of the ovary is quite unproven.*

5. Fourteen cases (9 well recorded) of ovarian tumour have been collected which are described and probably rightly described, in the majority of cases at any rate, as of "lutein" origin: (i) there is no essential clinical difference between them and the ovarian "hypernephromas" except that in the former some patients were pregnant and past pregnancies were more common. (ii) There is no essential macroscopic or microscopic difference between them and the ovarian "hypernephromas." Though glycogen and lumina are mentioned as frequently present in the latter—being wrongly regarded as evidence of their suprarenal origin—yet there are strong reasons for believing that both were also frequently present in the former; but no author who had once decided that his tumour was of lutein origin discussed even the

possibility of it being a hypernephroma, and consequently did not trouble to look for glycogen, or allude to the presence or absence of lumina.

6. As the small ovarian "hypernephromas" are now recognized to be lutein formations, so the majority if not all the large "hypernephromas" are probably also of lutein origin.

7. Suprarenal virilism was absent in the nine patients with "lutein" tumours who had not yet passed the menopause—which is evidence that they were not hypernephromas.

8. Though accessory suprarenals are relatively common in the broad ligament and its vicinity, only four alleged "hypernephromas" are recorded there, against ten large ones in the ovary. One alone produced suprarenal virilism and histologically appears like a suprarenal hypernephroma.

This is most probably the only true hypernephroma yet recorded in the female pelvis.

I am indebted to Dr. Adami for his interest in this paper and for helpful criticisms. I shall be grateful for sections of suprarenal hypernephroma.

APPENDIX.

Two recent cases of suprarenal virilism from inaccessible literature.

Case 1. A girl. (Hijmans, *Nederl. Tijdschrift voor Geneeskunde*, Jaargang, 1915, Tweede Helfe, No. 20, p. 2217). Abstract.

A girl, aged 3, came to the clinic with a large non-fluctuating tumour on the left side of the abdomen which moved with respiration—the duration of the tumour is not stated.

She was abnormally developed for her age; her height was 1.01 m., the average being .88 m.; her weight was 19.2 kg., the average being 14 kg. "Her expression was not youthful but fixed like that of an adult." Her speech was deliberate, her voice a deep alto. There was no hair on the face or axilla, but the pubic hairs were super-abundant and measured 4 cm. The breasts were not developed. The labia were enlarged and the clitoris bigger than that of an adult. She had never menstruated. Her skin was normal and unpigmented. An examination of the blood gave 4,168,000 erythrocytes per cmm.; 50 per cent. hæmoglobin, 9,400 white cells; polynuclears 56 per cent., large lymphocytes 6 per cent., small lymphocytes 30 per cent., large mononuclears and other forms 8 per cent.

X-Ray revealed a "normal" sella turcica. The tumour was removed by an operation but the patient died from shock shortly afterwards. The tumour was as big as a child's head and weighed 2,000 grammes; it was firm, orange-yellow and rather nodular owing to fibrous septa; the left kidney was atrophied, the right kidney normal, and the right suprarenal also normal.

Microscopically the tumour was composed of columns and groups of cells separated by connective tissue and sometimes by wide capillaries; the

cells had round nuclei and granular cytoplasms; they contained a large quantity of lipoid. When the columns were regular the growth resembled the suprarenal cortex. In some areas irregular giant cells with large deep staining nuclei were present; when the nuclei were close together and a cell outline indistinct the appearance was "syncytial." A drawing illustrates the giant cells with big hypochromatic nuclei like those photographed in Fig. 22.

Case 2. A woman. (Guemes, A., *Semana Medica*, Ano xxiv, No. 34, p. 207.) Abstract.

The patient, a woman—age not stated—was admitted under the care of Dr. Adolfo Guemes of the Rivadavia Hospital with debility, "hypochondria" and abdominal tumour. She had a beard and moustache of bristly hair; the top of her head was bald. Her body was covered with hair, especially developed on the forearms and linea alba. Her neck was thick and muscular. Her breasts were "withered." Her hands and feet were large and puffy like those in myxœdema. Her voice was deep. The clitoris was of "exaggerated" size.

The past history was as follows: Menstruation began at 20; she married young but had no miscarriages and no children. Two photographs of her are reproduced, taken 15 and 10 years before death; they show her face and figure was that of a normally developed *young* woman. Her illness began three years before death with amenorrhœa, associated with increasing swelling of the abdomen. Her voice deepened. Her weight increased by 12 kilos, *i.e.*, 26 lbs. in 6 months. Her muscles developed greatly, and her physical strength and capacity for work became such that she was able to carry out the duties of cook, charwoman, maid-of-all work and washerwoman! In the second stage of the disease her muscles diminished in volume and became flaccid; profound debility supervened and she was unable to work. The exact cause of death is not stated.

A post-mortem revealed a mammilated tumour of the right suprarenal gland weighing 141 grammes; it was pale yellow with hæmorrhagic and necrotic foci. Microscopically it was composed of alveoli of polyhedral cells with clear "spongy" cytoplasm, surrounded by fibrous tissue trabeculæ ramifying in from the capsule, or by thin-walled blood vessels which frequently ruptured. In some of the islets the cells had a "different appearance;" they were basophil with large hyperchromatic nuclei. Neither chromafin nor adrenalin were demonstrated in the tumour, but adrenalin was found in the left suprarenal gland. The liver was enlarged with numerous metastases, containing the two types of cells seen in the primary growth. There was a small adenoma of the thyroid showing on microscopical examination "colloid and hyaline degeneration." The ovaries were completely atrophied—microscopically sclerotic with small cysts. The pancreas and kidneys contained some sclerotic areas. The paper is illustrated with photographs of the patient before and after virilism developed, and with photomicrographs of sections of the various organs.

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Figs. 1 to 6 Reduced ⅓.

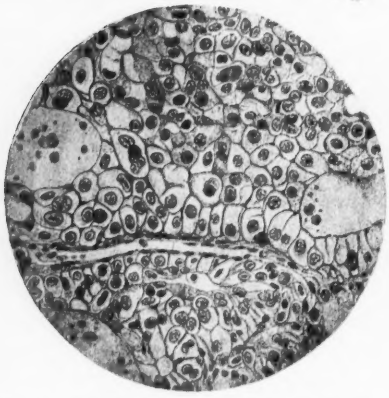

Fig. 1. Ovarian "hypernephroma," Case 1. (page 29).

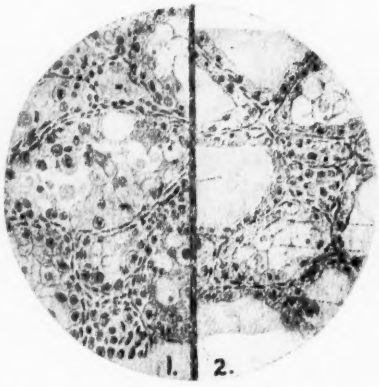

Fig. 2. Ovarian "hypernephroma," Case 9 × 300. (page 32).
1. Cells containing glycogen.
2. Cysts being formed.

Fig. 3. Ovarian "hypernephroma," Case 2. (page 30).

Fig. 4. Ovarian "hypernephroma," Case 7.
1. Tumour cells and capillaries. (page 32).
2. Tumour cells, capillary and blood.

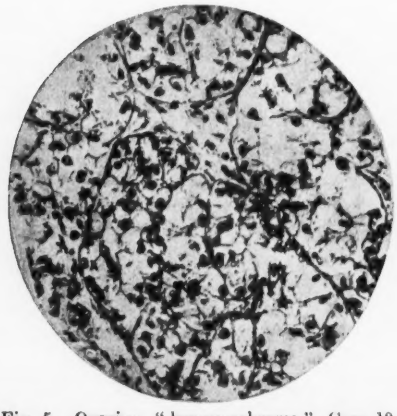

Fig. 5. Ovarian "hypernephroma," Case 10 (page 32).

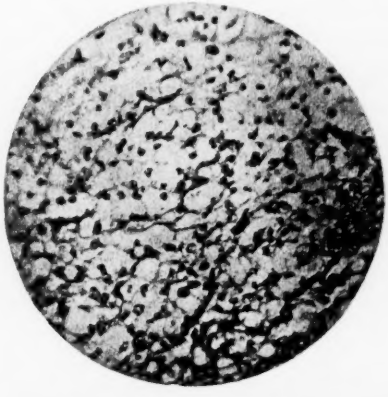

Fig. 6. Lutein tumour, Case 7. (page 39).

Figs. 7 to 12 Reduced ⅓.

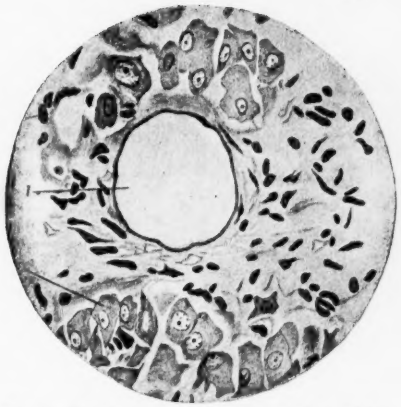

Fig. 7. Lutein tumour, Case 2. Ocul. 4, Obj. 4. Tumour cells, stroma and dilated lymphatic. (page 38)

Fig. 8. Lutein tumour, Case 6 × 400. Tumour cells and ovarian stroma. (page 39).

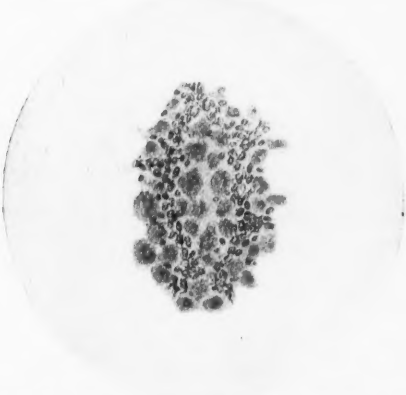

Fig. 9. Lutein tumour, Case 3. (page 38). Tumour cells and connective tissue stroma.

Fig. 10. "Hypernephroma" of broad ligament? Case 1. (page 54).

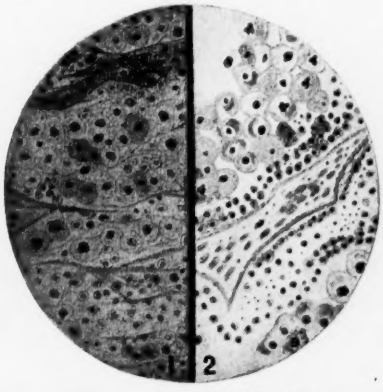

Fig. 11. "Hypernephroma" of broad ligament? Case 3, Ocul. 1, Obj. 6. (page 55).
1. Spongiocytes and dark cells.
2. Perivascular distribution of spongiocytes and dark cells.

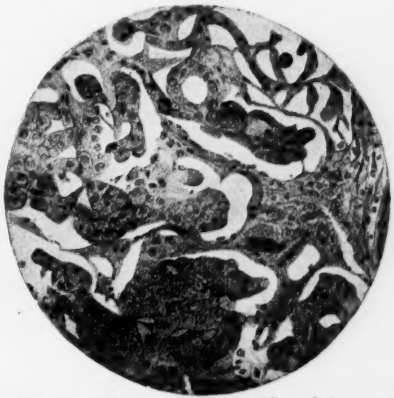

Fig. 12. "Hypernephroma" of broad ligament? Case 2 × 200. Tubular appearance of recently growing part. (page 54).

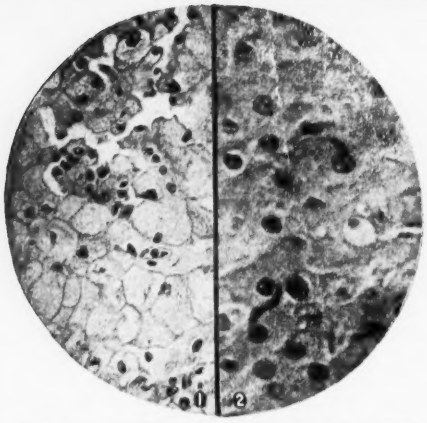

Fig. 13. 1. Renal "hypernephroma" × 300, alveolar type.
2. Small lutein tumour (Gordon) × 300.

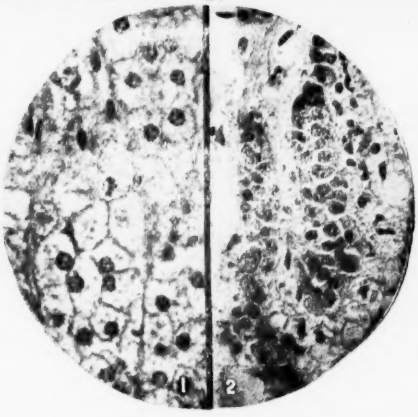

Fig. 14. Adrenal.
1. Zona fasciculata, much "fat"—usual.
2. Zona fasciculata, little "fat"—unusual

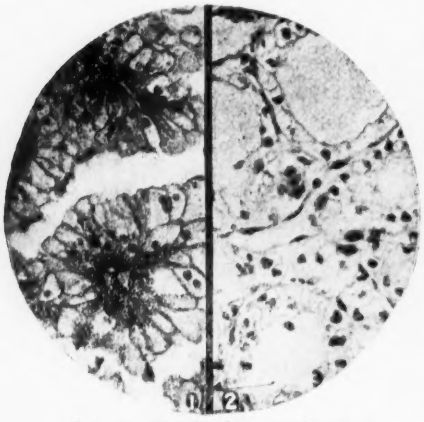

Fig. 15. Renal "hypernephroma."
1. Papillary type × 300.
2. Tubular type × 300.

Fig. 16. Adrenal hypernephroma × 300. Girl, sex changes (French).
1. Primary cells small; no vacuolation.
2. Metastasis cells smaller.

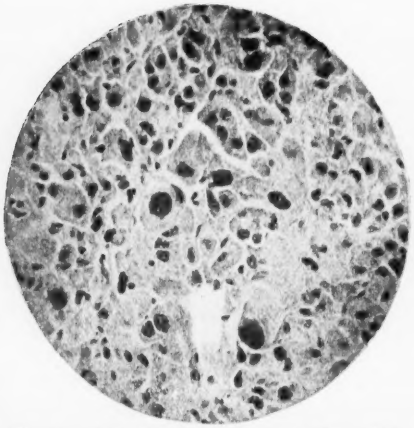

Fig. 17. Adrenal hypernephroma × 195. Girl, sex changes (Ritchie).

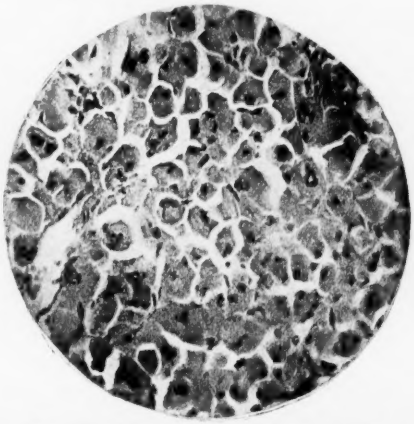

Fig. 18. Adrenal hypernephroma × 195. Woman, sex changes (Hewetson and Glynn); no vacuolation.

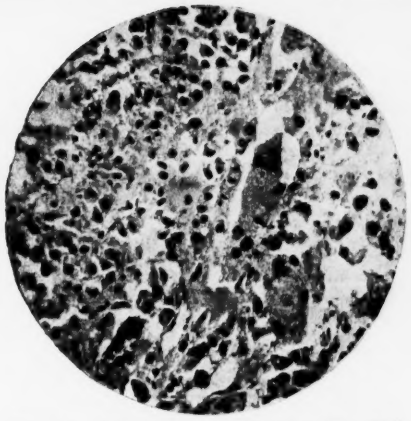

Fig. 19. Adrenal hypernephroma × 195 Girl, sex changes (Dun and Glynn). Note difference in cells right and left half.

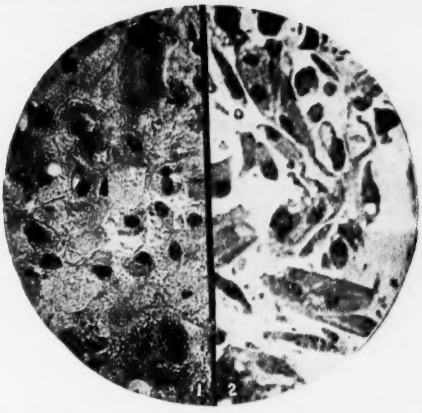

Fig. 20. Adrenal hypernephroma. Man (Kettle) × 300. Note difference in cells in same section, also slight vacuolation.

Fig. 21. Adrenal hypernephroma × 300. Girl, sex changes (Turnbull). Note differences in cells, also slight vacuolation in some.

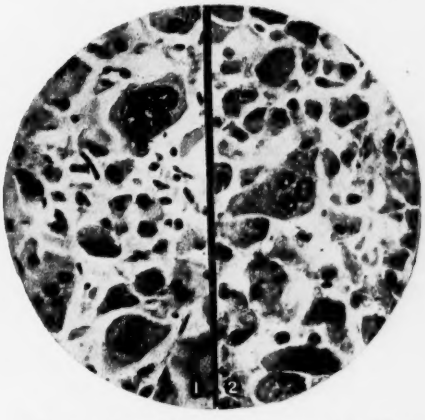

Fig. 22. Adrenal hypernephromas × 195. Note hyperchromatic and multinucleated cells. (1. Ritchie) (2. Dun).

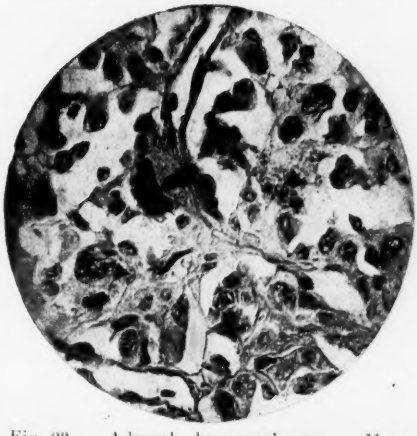

Fig. 23. Adrenal hypernephroma. Man (Thomas) × 300. Note excess of stroma found throughout section, cp. Fig. 24.

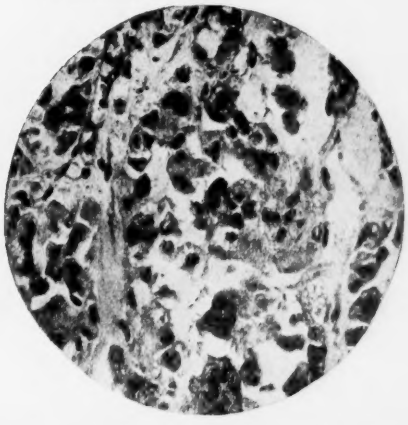

Fig. 24. Adrenal hypernephroma. Girl (Dun and Glynn) × 300. Excess of stroma in part of section, cp. Figs. 23, 19, 21, 22 (2).

Fig. 25. Adrenal hypernephromas × 300. Stroma visible from shrinkage.
1. Boy, sex changes (Adams).
2. Woman, sex changes (Hewetson), cp. Fig. 18.

Fig. 26. Adrenal hypernephroma × 300. Woman, age? (Spilsbury).
1 & 2. Different portions of same section, compare Fig. 16.

Fig. 27. Adrenal hypernephroma × 100. (French). Note perivascular arrangement and necrosis, cp. Figs. 16, 29.

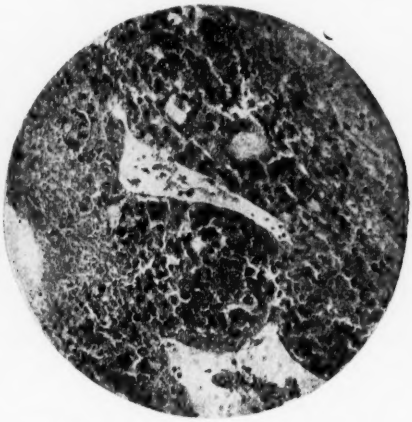

Fig. 28. Adrenal hypernephroma × 100. (Turnbull). Note perivascular arrangement and necrosis, cp. Fig. 27.

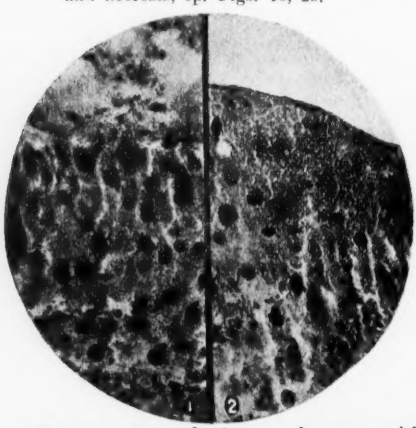

Fig. 29. Adrenal hypernephromas, girls, showing perivascular cells × 300. 1. French. 2. Turnbull.

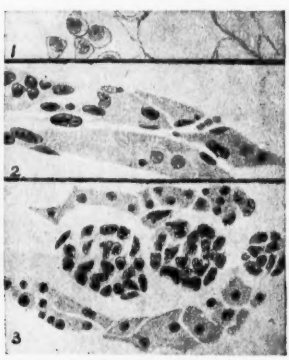

Fig. 30. Adrenal hypernephroma, man. (Woolley and Adami). Showing types of cells seen in Figs. 16 to 26. (Slightly reduced.)

Utero-Placental (Accidental) Hæmorrhage.

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PROLOGUE.

Since the commencement of July 1915 I have treated, or seen treated, and followed up, fifty cases of so-called accidental hæmorrhage and retroplacental hæmatoma.

Three of these cases have died, and have provided me with pathological material which I have carefully compared with other pathological material removed from women dying during labour from conditions other than accidental hæmorrhage.

This clinical and pathological material has stimulated me to attempt to place this condition on a satisfactory basis. The paper which has resulted consists of two parts—Part I, Clinical; Part II, Pathological.

PART I.

A CLINICAL REPORT OF FIFTY CONSECUTIVE CASES.

The ætiology of this condition is of considerable interest, and will be dealt with first. The average age-incidence in the series of fifty cases was 31.6 years, the youngest case being 19 and the eldest 43 years.

The parity incidence was as follows:—Nine (18 per cent.) were primigravidæ; 41 (82 per cent.) multiparæ. The average parity of the multiparæ was 5.7 pregnancies, with a maximum parity of 15 pregnancies. The abortion incidence was 1 abortion to 9 labours at term, as against a normal abortion incidence of 1 to 4 or 5 labours at term.

With regard to the causative factors, it will, I think, be best to take up separately the causes given by authors and eliminate them, when possible, singly. *Traumatism,* on careful questioning, played no part in any one of the cases. Neither did it in any of the 17 cases recorded by Whitridge Williams (1915).[35] It was thought to be the cause in a small percentage of Essen-Möller's (1913)[12] 29 cases, and in 5 of Gaston's (1906)[15] 70 cases. Frequently the patient attributed the hæmorrhage to an accident,

but the nature of the accident and the interval between the accident and the onset of symptoms always excluded it as the causative factor.

Rupture of the sinus circularis of the placenta is thought to be an occasional causative factor by Essen-Möller.[12]

Fright, morbus cordis, fibroid tumours and diseases of the blood played no part in any of the cases.

Shortness of the umbilical cord was not the causative factor in any one of the 50 cases. The average length of the umbilical cord in 32 cases in which it was measured was 21.3 in.; the longest being 34 in.; the shortest 13 in. In one case the cord is mentioned as having been wound three times round the child, but there was no tension on the cord, this child being born alive. Shortness of the cord was given as the cause in 12 of the 70 cases recorded by Gaston.[15] It appears to me impossible for shortness of the cord to cause separation of the placenta unless there is traction on the fœtus. Obviously the resistance by soft parts is such that the fœtus not only ceases to travel forwards at the time the uterine contraction ceases, but is actually forced backwards by the recoil of the muscular pelvic floor. During the pain the uterus with the placenta is travelling in the same direction and at the same pace as the fœtus is travelling. Therefore there can be no pull on the cord either during or at the termination of a pain, while the child remains within the genital tract.

Endometritis is, of course, an impossible ætiological factor to exclude, but if, as is generally stated, endometritis is a cause of abortion, the low abortion incidence would appear to negative this theory.

Syphilis. The Wassermann reaction was positive in only one of 15 cases in which it was applied. It will therefore be seen that syphilis played no part at any rate in these cases. It is mentioned as playing a part in one af Gaston's [15] 70 cases.

One condition, and one condition only, was pre-eminently associated with accidental hæmorrhage, *i.e.*, *albuminuria.* This was present in 42 (84 per cent.) of the 50 cases. The amount varied from a fine cloud to 15 parts per 1,000 (Esbach). It was usually, however, in considerable quantity. Hyaline and granular casts were present in 13 (26 per cent.) of the cases. Chronic nephritis was clinically present in only 3 (6 per cent.) of the cases. In the others, the albuminuria was apparently of toxæmic origin, *i.e.*, it cleared up after delivery, the average duration of albuminuria, excluding the chronic renal cases being 11.3 days. Toxæmic symptoms, *i.e.*, œdema, headache, vomiting, etc., were associated in 17 (34 per cent.) of the cases, eclampsia with one. This association of albuminuria cannot be looked on as an accidental

occurrence, and in the absence of other caustive factors, one naturally looks to the cause of the albuminuria as the cause of the hæmorrhage. The association of a toxæmic condition in a higher percentage of multiparæ than primigravidæ is, I know, without precedent, and I have no satisfactory explanation of this phenomenon. Winter, in 1885,[36] first directed attention to the presence of albuminuria in these cases, since which time nephritis or albuminuria has been regarded as the most constantly associated factor. It was associated with the condition in 64.7 per cent. of 17 cases (nephritis once) recorded by Whitridge Williams[35]; in 37 per cent. of 29 cases, Essen-Möller[12]; in 34.25 per cent. of cases recorded by Aschkanazy (1902)[1]; in 50 per cent. of cases, Muus (1903)[26]; in 42.86 per cent. of 70 cases, Gaston[15]; in 36.9 per cent. of 58 cases, Bar and Kervily (1906)[3] in 51.9 per cent. of 158 cases, Dorman (1913)[10]; in 50.75 per cent. of 67 cases, Hartmann (1907).[17]

The frequency of the condition in association with eclampsia has also been noticed, cases being recorded by Bar and Kervily,[3] Couvelaire (1912),[8] Essen-Möller,[12] Zarate (1915),[38] Seotz (1903)[30] and Young (1914)[37] amongst others. These figures, although in none of the records is the percentage as high as in my series, still further emphasize the association between albuminuria of toxæmic origin and utero-placental hæmorrhage.

The examination of the pathological material which I have obtained shows areas of necrosis with hæmorrhage in the uterine wall, and I formulate the following theory for the hæmorrhage: (1) Focal necrosis with hæmorrhage, in the musculature and decidua of the uterine wall; (2) resulting separation of an area of placenta opening the mouths of uterine sinuses; (3) extensive retro-placental hæmorrhage.

The onset of the hæmorrhage is usually towards the end of pregnancy. In this series there were between the twenty-third and twenty-eighth week, 3 cases; between the twenty-ninth and thirty-second week, 8 cases; between the thirty-third and thirty-sixth week, 11 cases; between the thirty-seventh and fortieth week, 24 cases.

The cases can be divided clinically into three groups: (*a*) Those in which the blood entirely escapes—*external cases;* (*b*) those in which the blood is entirely retained *in utero—internal cases;* (*c*) those in which there is free escape of blood with retention of a considerable amount *in utero—combined cases.*

Group (*a*): *External Cases.* These cases are infrequent. Among the series of fifty cases there were only seven belonging to this group. The hæmorrhage in these is never of great severity and is usually slight. The only symptom is bleeding, which comes on without cause. Repeated losses, as met with in placenta

prævia, do not occur. In the absence of labour pains there is no pain, but the bleeding is likely to bring on labour. On abdominal examination nothing abnormal is, as a rule, revealed, *i.e.*, the abdominal findings of placenta prævia are absent. The fœtal heart cannot be heard in about half the cases; its absence will assist the diagnosis, since in placenta prævia the child is usually alive at this stage. On vaginal examination nothing abnormal is revealed. If the cervix will admit the finger the placenta will not be felt. The presence of albumin in the urine will go far to confirm the diagnosis, but in the slight cases it is often absent. It was present in only two of the cases in this series. The diagnosis between this type of case and a lateral placenta prævia can usually only be made after the expulsion of the membranes and placenta, and then only when the bag of membranes is complete.

The Treatment. If the loss has been slight and has ceased, and if the child is alive, rest with a hypodermic injection of morphia will often result in the pregnancy continuing to term. The patient should be dieted and the bowels made to act two or three times daily for the remainder of her pregnancy with a view to elimination of toxin. If the loss is considerable, labour pains will always be present. The membranes should then be ruptured, a tight binder applied and a hypodermic injection of 1 cc. of pituitrin administered. If it is essential that no further loss should ensue, that is, if the condition of the patient is really serious, the vagina should be plugged with gauze in addition. With regard to plugging, I have had no case in which puerperal sepsis has followed its use. It has always been a routine that the vagina should be dried and swabbed out with iodine before plugging with dry sterile gauze. I feel, however, after my examination of pathological material that with plugging there is a risk of spontaneous rupture of the uterus through a necrosed area. This rupture actually happened in one case of combined hæmorrhage (*vide* Case 27) in which plugging was used.

. *Results.* If treatment is carried out along these lines bleeding will cease, labour will progress rapidly, and delivery will be spontaneous, the placenta and membranes as a rule following the baby at once. In this series of cases the results to the mothers have been uniformly good; the progress of labour having been satisfactory from the onset of treatment. Half the children were stillborn, but the life of the child is not under the control of the medical man, that being dependent entirely on the initial separation of the placenta.

(*b*) *Internal Cases.* These cases have been sub-divided into (1) clinical cases of internal hæmorrhage; (2) retroplacental hæmatomata.

(1) Cases of this class are also infrequent, occurring 11 times among the series of fifty cases. The hæmorrhage in these cases is always considerable, and this is undoubtedly the reason why the blood does not appear externally. The explanations for its non-appearance hitherto given are: (1) that the cervix is not dilated; (2) that the membranes are adherent around the internal os; (3) that the presenting part obstructs the canal; (4) that the blood ruptures into the amniotic sac. These are all unsatisfactory. With regard to the first of these explanations, it is well known that in threatened abortion there is bleeding in the absence of dilatation. Why not in this condition? To give as a definition of threatened abortion bleeding without dilatation of the cervix, and to give as a reason for internal hæmorrhage the absence of dilatation of the cervix, is a paradox which should have no place in obstetrical literature. As a point of fact, dilatation up to two fingers is often present in internal cases.

With regard to the second explanation—the adhesion of membranes—one has only to watch the delivery of a case of internal hæmorrhage to see that this plays no part. The placenta and membranes follow directly on the baby, and I have seen no case of combined or internal hæmorrhage in which this sequence of events did not occur. With regard to the third explanation; in the absence of rupture of the membranes it is obviously impossible for the presenting part to block the cervical canal. With regard to the fourth explanation, it appears to me to be mechanically impossible for the blood to rupture into the amniotic sac. For it to do so a sharp salient of membranes must project into the amniotic sac. The tension in the amniotic sac, normally not inconsiderable, will be raised at once by retroplacental hæmorrhage, and as fluid under pressure resists pressure equally in all directions, the formation of this salient will be rendered impossible.

The reason why the blood is retained is that the uterus is paralyzed. One assumes a sudden considerable hæmorrhage which forcibly distends the uterus which, thus taken unawares, becomes over-distended with resulting paralysis. The degree of paralysis varies from one in which, although the power of contraction is lost, the power of resisting further distension is retained—*i.e.*, muscular tone is present; to one in which all power is lost, the uterus becoming distended to the maximum stretching point of muscle; even this is occasionally overcome, the case then terminating in uterine rupture (*vide* Cases 4, 27 and 33).

Symptoms. The onset is sudden, with a severe or intensely severe pain in the abdomen. This is referred to by the patient as "indescribably bad," as "a tight band round the waist," or as a "bursting pain." The pain persists and there is no alleviation.

The patient's mental state is often so affected by its severity that she is incapable of giving a coherent history, but rolls about the bed complaining constantly of the agonizing pain. It was a marked symptom in 54 per cent. of the cases; but may be completely or almost completely absent. Vomiting is frequently present. It was present in 45 per cent. of the cases. It may be slight or persistent. The recognition of pallor by the patient or by her friends is a common symptom, and is helpful to the clinician. Fainting attacks, sometimes described as fits, are not infrequent. They were present in 45 per cent. of the cases.

An examination of the patient reveals anæmia, usually extreme. The face is blanched, the face and hands cold and clammy. The pulse varies from a normal good pulse to a running feeble pulse of 120 or more. The temperature is as a rule subnormal, the respiration rate is usually raised. The abdominal examination is characteristic, so much so that once palpated it is, I believe, difficult to fail to recognize a future case. The uterus is large; it may be definitely larger than it should be for the date of pregnancy. It is tense; this hardness is characteristic and resembles no other uterine condition. It is frequently, although not by any means always, tender; the tenderness may be localized to a definite area of the uterus. The fœtal parts cannot be recognized on palpation as a result of the hardness of the uterus. The fœtal heart cannot be heard. There are no uterine contractions. On vaginal examination the cervix may admit one or more fingers or may be undilated. The bag of membranes, if felt, is tense all the time, but not bulging. The urine will be found to contain albumin, which was present in every case in this series. The amount was never less than a cloud, and in only four cases less than four parts per 1,000 (Esbach). Granular and hyaline casts were frequently present.

Treatment. Attempts to stimulate the uterus are not only useless, but also tend to increase shock and should therefore not be encouraged. Attempts at delivery per vaginam will as a rule be fatal, and should play no part in the treatment of this condition. Rupture of the membranes is usually fatal, as it relieves the one thing that is keeping the bleeding in check, *i.e.*, the intra-uterine pressure, which has become greater than the patient's blood pressure. The treatment that I have adopted is to employ rest, and to watch carefully (1) the size of the uterus, which should be outlined with pencil; (2) the pulse; (3) the patient's general condition. The patient is put in bed and kept warm. If her pain is intensely severe she is given a hypodermic injection of morphia, $\frac{1}{4}$ grain. The fact that morphia masks symptoms must of course be taken into consideration.

If her condition improves she should be left, the pulse being taken and charted hourly, and the height of the fundus carefully noted. After a few hours' rest, the patient will recover from her shock, the uterus will recover from its paralysis, and contractions will start (vide Cases 35 and 43). The onset of contractions produces external loss, which should be looked on as a favourable sign, indicative of expulsive pains. The blood at first expelled is often watery, *i.e.*, serum stained with blood. This, I believe, is the origin of the theory that the blood has ruptured into the amniotic sac; the nurse in attendance has on more than one occasion informed me that the patient's membranes have ruptured, and that "bloody liquor" was coming away; examination has shown, however, an intact bag of membranes. When contractions are definitely present and there is external loss, the case can be treated as one of severe external hæmorrhage, *i.e.*, the membranes can be ruptured, the vagina plugged, a binder and perineal pad applied, and 1 c.c. of pituitrin administered hypodermically, or the case can still be left to nature. The former was done in one case with good result, the latter in five cases with excellent results.[1] The child will be expelled, stillborn, and will be at once followed by the flattened placenta, membranes and one or more pounds of clot.

If the patient's condition becomes worse, *i.e.*, if the pulse rises, the uterus gets larger, or her general condition becomes worse, the case can only be treated by laparotomy. Cæsarean section should be performed, and after removal of the fœtus, placenta, membranes and clot, vigorous attempts should be made to make the uterus contract (vide Case 33). This is usually possible with powerful hand and hot towel stimulation. If satisfactory contractions are produced, the uterus should be sutured. If it remains limp and flaccid, in spite of stimulation, it must be removed (vide Cases 37 and 41), preferably by subtotal hysterectomy. Good judgment is required in defining just when stimulation should be asserted to have failed. In Case 37 it was carried out for too long a period, the patient being allowed to lose more blood than she could afford to. After Cæsarean section and suture of the uterus it should be carefully examined for external partial ruptures (vide Cases 4 and 33). The presence of these will be shown by free intraperitoneal blood. These ruptures are due to the extreme tension, possibly coupled with necrosis, rupturing the peritoneum and the outer muscle layers, which contain more fibrous tissue than do the inner layers, and are also, of course, more stretched than are the inner layers. These tears should be sutured. The uterus should then

1. Since writing this paper I have seen four other cases treated by the latter method with equally good results.

be examined as a matter of interest for subperitoneal hæmorrhages, which are usually present, as are also intramuscular hæmorrhages, which may be noted at the time of Cæsarean section. The cases in which the uterus was sutured after Cæsarean section (Cases 3, 5 and 33) have all recovered, and Cases 3 and 4 have each had a live baby at term since, without untoward symptoms. The cases in which hysterectomy has been necessary (Cases 37 and 41) have died shortly after operation from the combined shock and loss of blood.

(2) *Retroplacental Hæmatoma.* By this term I mean hæmorrhages which are entirely behind the placenta, and are, as a rule, associated either with no external loss or only with a show. There were seven cases of this type in the series of fifty cases. They are clinically unrecognizable, but should always be suspected when, in a case of toxæmic albuminuria or chronic nephritis, intra-uterine death of the fœtus has occurred. They appear to be of particularly frequent occurrence in cases of chronic nephritis, the three chronic nephritis cases in this series all being in this class. There may be a history of a sudden short attack of pain, but more often there is a complete absence of symptoms. The condition is not of necessity associated with death of the fœtus, which will be dependent on the area of placenta separated. Albuminuria was present in all cases in this series.

Combined Cases. These cases are by far the most numerous. In the series of fifty there were twenty-five cases which came under this heading. Albuminuria was present in twenty-two of the cases, and was definitely absent in only two. Hyaline and granular casts were frequently present. The cases can be divided into two subgroups: (*a*) Cases of internal hæmorrhage in which recovery of the uterus has occurred almost at once, or at any rate before the patient is seen, so that when first seen she is losing blood; (*b*) Cases which have started with external hæmorrhage, but in which a sudden severe hæmorrhage has caused paralysis of the uterus, with consequent cessation of loss.

(*a*) These cases are by far the most frequent. They show a combination both in symptoms and signs of internal and external hæmorrhage. There are, as a rule, abdominal pains, vomiting, anæmia, and often fainting attacks, followed, either at once, or after a short interval, by bleeding. In some cases these symptoms, with the exception of bleeding, are not present, and only the characteristic uterus indicates the presence of internal hæmorrhage. The treatment is on the lines of an internal hæmorrhage after external bleeding has started, *i.e.*, either the case is left to nature or the membranes are ruptured, a tight binder is applied and a hypodermic injection of 1 c.c. of pituitrin administered, or the above

are associated with vaginal plugging. The results to the mothers have been with one exception excellent; one case dying of uterine rupture (vide Case 27). The children have been with three exceptions stillborn.

(*b*) These cases are rare. It is obviously improbable that the uterus will become distended after labour has once started. They are recognized by the characteristic signs of internal hæmorrhage following on external hæmorrhage. The treatment is that of internal hæmorrhage, that is, the treatment of the state present. The results should be satisfactory to the mothers.

Briefly summarized the cases have been as follows:—

	Cases.	Incidence of Albuminuria.	Maternal Mortality.	Fœtal Mortality.
External bleeding	7 (14%)	2 (28%)	0	4[1] (56%)
Internal bleeding	11 (22%)	11 (100%)	2 (18%)	11 (100%)
Combined bleeding	25 (50%)	22 (88%)	1 (4%)	22 (88%)
Retro-placental hæmatoma ...	7 (14%)	7 (100%)	0	3 (42%)
Total	50	42 (84%)	3 (6%)	40 (80%)

To Mr. Comyns Berkeley and Mr. Eardley Holland my best thanks are due for permission to publish the cases treated at the City of London Maternity Hospital. To Dr. Russell Andrews my best thanks are also due for permission to make use of, and publish, certain cases occurring at the London Hospital. Dr. Russell Andrews was extremely kind in allowing me to see and treat cases of utero-placental hæmorrhage in the London Hospital which were under his care, and for this and other kindnesses I am greatly indebted to him.

RESULTS OF TREATMENT.

	(1) None.				(2) Membranes ruptured; tight binder; pituitrin.			
	Mother.		Child.		Mother.		Child.	
External bleeding	4	G (4)	G (3)	SB (1)	—	—	—	—
Internal bleeding	5	G (5)	—	SB (5)	1	G (1)	—	SB (1)
Combined bleeding ...	10	G (10)	G (3)	SB (7)	5	G (5)	—	SB (5)
Retro-placental hæmatoma...	6	G (6)	G (3)	SB (3)	—	—	—	—

	(3) Membranes ruptured; tight binder; pituitrin; plugging of vagina.				(4) Forceps delivery.			
	Mother.		Child.		Mother.		Child.	
External bleeding	1	G (1)	—	SB (1)	—	—	—	—
Internal bleeding	—	—	—	—	—	—	—	—
Combined bleeding ...	8	G(7) D(1)	—	SB (8)	1	D (1)	—	SB (1)
Retro-placental hæmatoma...	—	—	—	—	—	—	—	—

1. Two died after delivery.

	(5) Leg brought down.				(6) Cæsarean section.				(7) Cæsarean hysterectomy.			
	Mother.		Child.		Mother.		Child.		Mother.		Child.	
External bleeding	2	G(2)	—	D(2)	—	—	—	—	—	—	—	—
Internal bleeding	—	—	—	—	3	G(3)	—	SB(3)	2	D(2)	—	SB(2)
Combined bleeding	1	G(1)	—	SB(1)	—	—	—	—	—	—	—	—
Retro-peritoneal hæmatoma	—	—	—	—	1[1]	G(1)	G(1)	—	—	—	—	—

PART II.

THE PATHOLOGY OF UTERO-PLACENTAL (ACCIDENTAL) HÆMORRHAGE.

(From the Pathological Institute of the London Hospital. Prof. Hubert M. Turnbull.)

REVIEW OF LITERATURE.

The pathological work carried out by numerous investigators has been considerable. The uterine musculature, blood vessels and decidua, and the placenta have come under notice and, further, studies of the other organs at necropsy have been made. It seems best to take up these structures separately, and briefly to record the conditions noted by different investigators. The uterine musculature has been particularly studied by Couvellaire (1911),[9] Essen-Möller,[12] Whitridge Williams,[35] Zarate,[38] Seitz,[30] and von Weiss (1897),[34] The decidua by Seitz,[30] von Weiss,[34] Schickele (1904),[29] Zarate,[38] and Biancardi (1905).[5] The uterine blood vessels by Whitridge Williams,[35] Seitz,[30] von Weiss,[34] and Essen-Möller.[12] The placenta by Young,[37] Biancardi,[5] Seitz,[30] and von Weiss.[34] The organs at necropsy by Couvellaire,[8] Bar and Kervily,[3] Hartmann,[17] and von Weiss.[34]

The Uterine Musculature.

Macroscopically, peritoneal ruptures and external, superficial ruptures of the myometrium have been noted by von Weiss,[34] Kouwer (1908,[23] Hicks (1861),[18] Engström (1911), Lieven (1914),[24] Zweifel (1912),[32] and Shaw (1914),[31] and have been given special attention by Knauer (1903),[22] who attributed them to sudden severe distension, and by Fraipont (1914),[14] who attributed them to intramuscular hæmorrhages, diminished elasticity and friability of the uterine wall.

Inter- and intra-fascicular hæmorrhages in the uterine musculature. "*Apoplexie utero-placentaire.*" (Couvellaire (1912.)[8]

1. Operation performed for eclampsia.

These have been noted by numerous authors, particularly by Couvellaire,[8] who first accurately described the condition. Secondly by Zarate,[38] Fabre and Bourret 1912),[13] Zweifel,[32] Berggren (1912),[4] Spaeth (1913),[28] Jettner (1913),[19] Fraipont,[14] Clifford (1914),[7] King (1914),[21] Young,[37] Brandt (1914),[6] Shaw,[31] Knauer,[22] Seitz,[30] Targett (1905),[33] Le Lorier (1906),[25] Bar and Kervily,[3] Keyworth (1909),[20] Munro Kerr,[27] and Whitridge Williams.[35] Hæmorrhages into the broad ligaments and Fallopian tubes have also been described by Couvellaire,[8] Whitridge Williams,[35] and Berggren.[4] Whitridge Williams described an extensive hæmorrhage into the right ovary, and Couvellaire described, and illustrated in colour, one case in which there were numerous punctiform and streaky hæmorrhages into both ovaries. Microscopically the hæmorrhage into the uterine wall is described by all authors somewhat as follows:—

The muscle bundles are separated and split into little bundles by streaks of red blood cells which dissect the individual bundles and, indeed, often separate cell from cell. These hæmorrhages are sometimes more numerous near the peritoneum, sometimes near the decidua. They are usually more numerous in the region of the placental site. Zarate[38] recorded one case which appears to me to be of great importance in that it gives evidence of the presence of focal hæmorrhages and necroses which preceded the accidental hæmorrhage. In a case of accidental hæmorrhage associated with eclampsia which came to necropsy he found both recent and old hæmorrhages in the uterine musculature. To quote from his paper:—"The antiquity of some of the hæmorrhages is shown by their differential colouration with eosin. The attention is attracted by the great quantity of connective tissue surrounding degenerated muscle bundles. This degenerated tissue, associated with an infiltration by round cells, is most noticeable in the areas in which older hæmorrhages are." This means, I take it, that there have been an infiltration and replacement by fibrous tissue of degenerated muscle in the region of the older hæmorrhages.

Œdema of the inter-fascicular connective tissue has been described as frequently present by many of the authors especially by Couvellaire[9] and Whitridge Williams.[35]

Leucocytic infiltration of the musculature is noted particularly by von Weiss,[34] who held that it was the cause of the condition. In his specimens the inner layers of the uterine musculature showed the most marked leucocytic infiltration, that in the outer layers being of the nature of a perivascular infiltration. It is important to add that in 4 out of the 5 cases in which the uterus was examined it had been plugged during life with iodoform gauze. This of itself would give rise to leucocytic infiltration. The case that was

not plugged showed the least leucocytic infiltration. Two of his cases showed an increase in the connective tissue of the uterine wall. Leucocytic infiltration of the musculature of slight degree around the older hæmorrhages is also recorded by Zarate[38] in one case, to a slight extent beneath the decidua in one case by Seitz,[30] and in one case to a slight extent with a perivascular distribution by Couvellaire.[8] It is recorded as being absent by Berggren,[4] Essen-Möller,[12] Couvellaire,[8] and Whitridge Williams.[35]

Degeneration of the individual muscle fibres is recorded by Seitz[30] in two cases, by Hartmann[17] and by Zarate[38] in one case, who said "some of the muscle fibres were entirely degenerated. Others showed the characteristic vacuolation of fatty degeneration." Degeneration was not noted by Couvellaire,[8] Essen-Möller,[12] Whitridge Williams[35] or Young.[37]

The Uterine Blood Vessels.

Changes in the blood vessels were noted by Whitridge Williams[35] and Seitz.[30] They were found in the smaller blood vessels by Whitridge Williams in two cases, who thus described them: "In some of the smaller arteries the intima was swollen and projected into the lumen. It was conspicuous on account of the diffuse blue staining which it assumed. In such areas the finer architecture of the vessel wall was disturbed and peculiar defects were seen which appeared as clear circular or elliptical zones, while in other places irregular blue granules were formed which stained very intensely with hæmatoxylin. Throughout these areas nuclear fragmentation and atypical arrangement of cells was observed. In several places defects were present in the intima of the larger arterioles which may have been connected with the hæmorrhagic areas in their vicinity. In the walls of many of the larger veins free hæmorrhage had occurred, just beneath the endothelium, which communicated freely with the hæmorrhagic effusions between the muscle fibres. Similar changes did not exist in the main blood vessels." "In conclusion," he said, "careful study of the arterial lesions in my specimen has led me to believe that they are toxic in origin and are due to the action of some substance circulating in the blood which possibly also produces changes in the smallest arterioles and capillaries which permit the escape of blood into the tissues just as is observed in certain varieties of snake poisoning."

Seitz found changes in the blood vessels beneath the placenta of the nature of a marked proliferation of the vascular endothelium with narrowing of the lumen.

The vascular changes described by Seitz, and the changes in

the vessels, apart from hæmorrhage, which were described and figured by Whitridge Williams, appear to me to be identical with those which normally take place in the sub-placental vessels at or about term, and which have been described in full by Goodall (1910).[39] Lacerations of the walls of some of the blood sinuses were noted by Couvellaire.[8] By many authors the blood vessels are described as being normal, noticeably by Couvellaire,[8] Berggren,[4] Essen-Möller,[12] Fabre and Bourret.[13]

The Decidua.

Hæmorrhage into the decidua has been noted by all observers. Such hæmorrhage is a natural association of labour.

Leucocytic infiltration of the decidua has been noted by many observers, especially by von Weiss,[34] Seitz,[30] who recorded its presence in one case but not in another, and Biancardi,[5] who described it as more or less well marked in two of nine cases. Von Weiss in several of his cases found extreme leucocytic infiltration of the uterine but not of the placental decidua. This infiltration was conspicuous only in the cases in which the uterus had been packed with iodoform gauze and was present in all such cases. There can be little doubt that the packing was responsible for the infiltration. Inflammatory decidual changes were not present in the cases described by Couvellaire,[8] Essen-Möller,[12] Whitridge Williams,[35] Gottschalk (1897)[16] and Zarate.[38] No micro-organisms were found by any observer.

Degenerative changes in the decidua were observed by Seitz,[30] who considered the retro-placental hæmorrhage to be a phenomenon secondary to decidual necrosis or inflammation. He stated that "when the hæmatoma is intra-placental the decidua is still necrosed. Such necrosis cannot be due to compression by the hæmatoma. We have found the cause of the pathological changes in the placenta to reside in the inflammation and degeneration of the decidua basalis." He considered the degeneration of the decidua, which he found most marked in the decidua basalis, to be due to vascular changes or chemico-toxic influences. Von Weiss[34] described extensive decidual necrosis in one case, focal decidual necrosis in two cases, and no necrosis in two cases. The necrosis when present was always most marked in the decidua basalis. Decidual degeneration was also ascribed by Schickele,[29] who attributed it to a lack of blood supply to the decidua by which means a slow necrosis was produced. This lack of blood supply he considered to be in part the result of uterine contractions, in part the result of thrombosis of the sub-placental sinuses. He said that "owing to the lack of knowledge of the changes in the blood

vessels towards the end of pregnancy one was not able to attribute the decidual changes (necrosis) to pathologic changes in the blood vessels, but there is a definite poverty of blood vessels in the region of the placental site. There is seen a defective nutrition of the decidua and a slow necrosis."

Biancardi,[5] in 9 placentæ from cases of accidental hæmorrhage, found in the decidua hæmorrhagic foci in various stages of retrogression, deposits of fibrin, distension and thrombosis of blood vessels, and thickening and degeneration of the decidual elements, varying from cloudy swelling to complete necrosis. "These changes are," said he, "always more marked in the region of placental detachment." He considered the decidual degeneration to be the cause of the placental changes which he described in detail. He admitted, however, that, apart from hæmorrhages and leucocytic infiltration, these decidual changes are found in the decidua of the normal placenta. He attributed the decidual degeneration to deciduo-ovular toxic products or fœtal toxins.

Gaston [15] found that Nitabuch's fibrin layer was thickened and the decidual cells were blurred and contained poorly stained nuclei. He considered that decidual hæmorrhage was the primary cause of placental separation. Gottschalk [16] found "extensive decidual degeneration in excess of the normal with focal areas of complete necrosis. Emboli, some recent some old, in the decidual blood vessels." He considered that the thrombosis was secondary to necrosis of the vessel walls, and that this in turn was secondary to defective decidual blood supply. The hæmorrhages he attributed to local increase of blood pressure, the result of occlusion of capillaries. He was of opinion that "the kidney of pregnancy" and retro-placental hæmorrhage were secondary to decidual necrosis, this in turn being due to defective blood supply. The renal changes he considered to be set up by liberated albuminuric poisons.

Placental Changes.

The changes in the placenta have deen described by many authors. They consist purely of the various stages of infarction. These changes have been carefully studied by James Young.[37] Apart from stages of infarction, which are mentioned by all authors, little has been described. Essen-Möller[12] stated that the degenerative changes found in the placenta are not characteristic of uteroplacental apoplexy but may occur in other conditions as well. Gaston[15] found thick vessels in the villi but no peri- or endarteritis. Seitz[30] found round-celled infiltration of those villi which lay in contact with the degenerated decidua, and considered this to be "inflammatio per contiguitatem." He also noted fibrous hyper-

trophy of von Franque (concentric stenosis) of the vessels in villous stems near infarcts, and considered such hypertrophy as secondary to vascular stenosis and occlusion in the infarcted area. He further found syncytial hyper-activity in one case. This latter condition was also noted by von Weiss[34] in two cases. The paucity of changes described in the placenta, apart from those due to infarction, is noteworthy, when one considers the numerous changes described by various authors in the other structures discussed.

Changes in other Organs.

Excluding those cases in which the condition was associated with eclampsia there are not many recorded cases in which changes in the organs are described. Bar and Kervily[3] recorded a case which is of such importance that I quote it at length.

A vi-gravida; 30 weeks pregnant. A typical case of internal hæmorrhage treated by de Ribes' bag. Patient became worse. Cæsarean section performed. Uterus contracted well. Sutured. Death. Necropsy: the liver was pale and yellowish suggesting an early fatty change. The centres of the lobules appeared as yellow dots. There were no hæmorrhages. Microscopically in the portal zones the liver cells were normal. In the central zones the liver cells were shrunken and often ragged. The cytoplasm was pale, the nuclei (sometimes free, sometimes only surrounded by a little shrunken cytoplasm) were shrunken and pale or hyperchromatic. The area affected was the inner half of the lobule. Sections stained with osmic acid showed fine fatty granules in the cells throughout the liver but more numerous in the cells around the central veins. The kidneys were large and pale. There was granular degeneration of the cytoplasm of some of the cells of the convoluted tubules. There were casts in the tubules of the loop of Henle.

Bar and Kervily arrived at the following conclusions from this case that " if researches show that hepatic lesions similar to these are characteristic of utero-placental apoplexy it will be proved that retro-placental hæmorrhages are not merely vaguely allied to nephritis but are directly allied to a complex state which one of us, Bar calls eclampism."

Von Weiss[34] found degeneration of the renal parenchyma in three cases. In one the epithelium was swollen; there were hæmorrhages and granular discoloured hyperæmic foci devoid of nuclei. In one there were swelling and focal necrosis of the epithelium of the convoluted tubules. In one there were swelling and granular opacity of the epithelium of the convoluted tubules, the lumina being frequently occupied by shed cells; there were also focal areas of destruction of cells and disappearance of nuclei. The

same author found liver changes in two cases. In one the liver cells were swollen and discoloured; in the other the cells were large and swollen. In this case he also recorded sub-endocardial ecchymoses.

Knaeur[22] found sub-endocardial ecchymoses in the left ventricle in one case, sub-acute nephritis with hæmorrhage in the second case, and chronic nephritis with atrophy of the kidneys and hæmorrhages into the liver in the third case. Hartmann[17] found fatty infiltration in the liver and, in one case, small blood extravasations in the liver without necrosis or thrombosis.

PERSONAL OBSERVATIONS.

The material at my disposal consisted of three uteri removed for accidental hæmorrhage from Cases 27, 37 and 41 of my paper upon the clinical phehomena, of the kidney and liver of Case 27, the kidney of Case 37 and of the kidney, liver, myocardium, diaphragm and spleen of Case 41. In one of these uteri there was spontaneous rupture. Further, I have taken as controls five uteri removed, at or near term, before or after death: (1) A uterus removed by operation from a case of rupture, the result of obstructed labour due to an impacted breech presentation with extension of the legs. (2) A uterus removed by operation from a case of rupture due to obstructed labour. (3) A uterus from a case of placenta prævia in which, during the performance of bi-polar version, the placenta was widely separated. A leg was then brought down. The uterus was at the time in a state of atony produced by chloroform. There resulted, therefore, extensive intra-uterine hæmorrhage, which caused the death of the patient in less than a quarter of an hour. The uterus was removed immediately after death and showed no macroscopical change. (4) A uterus removed by operation from a case of rupture. In this case there was no absolute obstruction although there was considerable delay and slow advance due to a minor degree of contraction of the pelvic outlet. There was, further, a very considerable degree of albuminuria, which disappeared after removal of the uterus. (5) A uterus removed post mortem from a case of rupture extending from a traumatic laceration produced by a manual dilatation of the cervix.

These two series of cases have been divided into two groups, (A) cases of accidental hæmorrhage, (B) control cases.

In the following description of the macroscopic and microscopic changes, the macroscopic reports of the control cases are omitted, because in these no macroscopic change was observed, except hæmorrhage and œdema along the edge of the rupture.

GROUP A.

Cases of Accidental Hæmorrhage.

Case A1. S.D. 1170, 1917 (Case 27 of Appendix, Part I).

MACROSCOPICAL EXAMINATION.

A uterus 16 cm. long by 12 cm. from side to side by 8.5 cm. from before backwards. Its inferior limit is, on the posterior surface, a horizontal line of operative incision 8 cm. long. The rest of the inferior limit is represented by a ragged tear with thinned edge. This tear passes through the lower uterine segment and is horizontal save to the left where there projects downwards a triangular tongue of tissue measuring 7 cm. in length and 3 cm. across its base; the apex of this tongue is part of the cervical lip. There is subperitoneal blood infiltration extending upwards from the edge of the tear for a distance of 5 cm. upon the anterior wall. A similar infiltration is present throughout both broad ligaments and extends inwards beneath the uterine peritoneum of the posterior surface for a distance of 5.5 cm. on the left side, and 4 cm. on the right side. There are faint, irregular subperitoneal hæmorrhages (up to 1 cm. diameter) scattered over the anterior wall of the upper body and over the fundus uteri. The muscularis varies from a thickness of 5 cm. at the fundus to 2.5 cm. at the lower limit. A central vertical section reveals:—In the muscularis of the fundus, at a depth of 1 cm. from the peritoneal coat, an irregular hæmorrhagic area 2.5 cm. long by 0.3 cm. deep; in the anterior wall a hæmorrhagic area 8 cm. from above downwards by 2.5 cm. deep. The latter hæmorrhagic area involves the total depth of the wall save for the outer 2 cm. and the inner 0.5 cm.; it is slightly raised above the surrounding cut surface and crimson in colour, finely mottled towards its inner margin with translucent grey; it is considerably softer than the surrounding muscularis; it is limited internally by a very definite wavy band of more swollen, less hæmorrhagic, pinkish grey, soft muscularis. Two cm. above the horizontal tear there is a small, irregular, ill-defined hæmorrhage (0.9×0.3 cm.). Parallel vertical sections show even more extensive hæmorrhage than in the areas described. The placental site is situated upon the anterior wall; it measures 6×5.3 cm. and lies internal to the hæmorrhagic area in the anterior wall. The lower margin of the placental site is 6 cm. above the edge of the tear. The tubes and ovaries are normal. There is a corpus luteum (1.4×1 cm.) with glossy fibrous centre (0.6 cm. diameter) in the left ovary.

A piece of liver (5.5×3×0.8 cm.). It is clay coloured. The parenchyma is swollen; the lobular pattern distinct. The periphery of each lobule is outlined by a pale brown rim.

Two portions of kidney (5.5×2.7×1.2 cm.). The capsule is thin, and the stripped surface perfectly smooth. The cortex, 0.8 cm. deep, is swollen, clay-coloured and flecked with very small, faint, paler dots. The cortical pattern is indistinct. The medulla is 1.2 cm. deep.

MICROSCOPICAL EXAMINATION.

Portions were embedded in paraffin and after cutting were stained with

1. The letters S.D. and P.M. and the numbers following them refer to the Ledgers of the Pathological Institute of the London Hospital. S.D. Surgical Department P.M. Post-mortem Department.

Ehrlich's hæmatoxylin and eosin, with Weigert's iron hæmatoxylin and van Gieson's mixture, and with Weigert's fuchsin and neutral red. Other portions were cut upon the freezing microtome, and sections were stained with Sudan III and hæmatoxylin. Sections (*a*), (*b*), and (*c*) were taken from the anterior wall of the uterus, (*d*) from a small hæmorrhagic area at the fundus, (*e*) from the placental site, (*f*) from an area free from hæmorrhage, (*g*) from the edge of the tear in the uterus, (*h*) from liver, (*i*) from kidney.

Section (*a*). *Anterior wall of uterus.* The surface is formed by a narrow zone of decidua vera. Throughout this the cells are dissociated to a greater or less degree and many are shrivelled and devoid of nuclei. This dissociation in places appears to be due to œdema, clear spaces separating the cells; elsewhere the interstices between the cells contain red blood corpuscles. Necrosis is greatest in the areas of hæmorrhage. In the inner sixth of the myometrium the individual muscle fibres cannot be distinguished, but the bundles are represented by a vacuolated matrix in which lie a very few tortuous narrow hyper- and hypochromatic nuclei. The veins are engorged and there are a few areas of hæmorrhage. In the remainder of the inner third a few portions of the muscular bundles show similar degeneration and necrosis. Here, in the majority of the muscle bundles, the cells are not shrivelled but are swollen; they are seldom clearly defined, and absence of nuclei is conspicuous. There are many hæmorrhages; these hæmorrhages are for the most part in the fibrous intermuscular septa. The degeneration and necrosis do not bear a fixed relation to the hæmorrhages. In the middle and outer third the changes in the muscle are very similar; defined cells are more numerous but the majority of these are greatly vacuolated; others are hyaline. There are hæmorrhages in the middle and outer third; they are more numerous in the middle third, but here are scanty in comparison with those in the internal third. In the outer sixth the bundles are widely separated by œdema.

There is an infiltration with leucocytes throughout the decidua, the infiltration being greatest where hæmorrhage is absent. There is considerable infiltration throughout the myometrium. It is chiefly perivascular, lying near veins and capillaries. The majority of the infiltrating cells have a round of oval nucleus and a basophil cytoplasm which is frequently vacuolated; there are also a very few neutrophil leucocytes.

In sections stained with Sudan III fat granules are demonstrated in the endothelium of a few capillaries and in a very few of the infiltrating cells, but not in the muscle fibres. There is a musculo-elastic hypertrophy of the intima of the larger arteries.

Section (*b*). *Anterior wall of uterus.* This section includes the decidua vera. The majority of the muscle bundles in the inner third of the myometrium show degeneration and necrosis similar to those already described. In the central third of the myometrium the fibres in a few bundles are ill-defined and vacuolated or shrivelled, but few have lost their nuclei. In the outer third are very few fibres which are not sharply defined and apparently healthy. There are hæmorrhages in the decidua and several hæmorrhages in the inner third of the myometrium. In the central third there are a few areas of hæmorrhage, and in the outer third are a very few small hæmorrhages. The hæmorrhages are found in areas of degenerate muscle, but there is much muscular degeneration independent

of hæmorrhage. In the outer third, greatest in the outer sixth, is an œdematous separation of the muscular bundles. Cellular infiltration, similar in character and distribution to that seen in the last section, is present. The decidual veins are partly closed by intimal proliferation. Fat is confined to a very few endothelial and free granule-cells.

Section (*c*). *Anterior wall of uterus.* This section also includes the decidua vera. Muscular degeneration and necrosis are more extensive than in either of the two preceding sections. They again increase in amount from without inwards, almost the whole of the inner third of the myometrium being affected. Hæmorrhages are confined to the decidua and inner third of the myometrium. Œdematous separation of muscle bundles is again conspicuous in the outer third. The cellular infiltration is also present. There are numerous polygonal and small, narrow, spindle cells loaded with fat in the interstitial tissue of the inner third of the myometrium; similar cells are scattered throughout the outer two-thirds. A very few of these spindle cells are of larger size, and may be atrophied muscle fibres.

Section (*d*). *Fundus of uterus.* A portion of myometrium from fundus uteri. In the inner third are extensive necrosis and degeneration of the myometrium together with slight œdema. In the central third the degeneration is slightly less and the œdema is greater. In the inner half of the outer third separation of the muscle bundles by œdema is very conspicuous, the muscle fibres here are less degenerated but are for the most part very narrow, pale and ill-defined. In the outer half of the outer third there is little evidence of œdema or of muscular degeneration. There are a few hæmorrhages into the interstitial tissue of the middle third. In the outer third, in both its outer and inner halves, there are numerous large hæmorrhages. Slight cellular infiltration is again present.

Section (*e*). *Placental site in uterus.* In the decidua basalis wide venous spaces are filled by red blood and clot. There is much hæmorrhage into the decidual tissue. In the inner third of the myometrium degeneration and necrosis of the muscle are extensive. A conspicuous feature is the different degree to which different fibres in one and the same bundle are affected. Thus, there are many bundles in which groups of fibres are swollen, hyaline and nucleated, whilst the remaining fibres are represented by a vacuolated area almost or completely devoid of nuclei (Fig. I). The nuclei in the hyaline fibres are pyknotic. Vacuolated hyaline fibres are also present. In the central and outer third similar degeneration and necrosis are present but are of much less degree. There are no hæmorrhages. Infiltration with neutrophil leucocytes is very great in the decidua and is conspicuous in the inner muscularis. Towards the serosa the infiltration decreases, and lymphocytes become much more numerous than leucocytes.

There are many round and polygonal cells loaded with fat in the decidua. In the myometrium there is a considerable number of fat granule cells in the interstitial tissue. Narrow spindle cells containing fat also lie between and parallel to the fibres in many bundles of muscle. In transversely cut muscle bundles the majority of these cells are triangular or stellate and lie between muscle fibres. They belong to the interstitial tissues and some at any rate represent the endothelium of capillaries.

Section (*f*). *Non-hæmorrhagic uterus.* In this section degeneration of the myometrium is much less obvious. In many bundles, however, and

more especially in portions of bundles, the muscle fibres are greatly vacuolated. The vacuolation is associated with karyolysis. Hyaline degeneration is very rare. The degeneration is slightly greater in the internal and central thirds. There is no hæmorrhage save in the decidua. The decidua is infiltrated with neutrophil leucocytes, lymphocytes, and plasma cells. In the myometrium there is a slight perivascular infiltration with lymphocytes, larger epithelioid cells and plasma cells. The cytoplasm of some of the epithelioid cells is vacuolated.

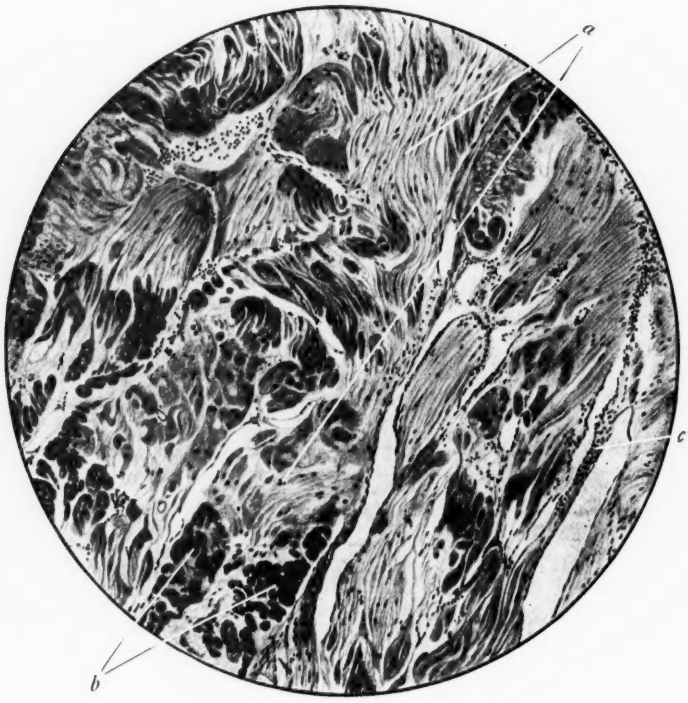

FIG. I.

S.D. 1170/1917.

Section of inner third of myometrium showing (*a*) extensive areas of degeneration and necrosis; (*b*) scattered focal islets of healthy muscle fibres, and (*c*) perivascular leucocytic infiltration.

Section (*g*). *Edge of tear in uterus.* A section taken at right angles to the long axis of the tear. It includes endometrial and peritoneal surfaces for about 2 cm. to the side of the line of cleavage. The decidua drops towards the line of cleavage so that the line of cleavage measures in depth one-quarter of the depth of the uterine wall at the other end of the section. For four millimetres from the line of cleavage the whole wall is represented by a few small islands of degenerate and necrosed muscle; narrow dissociated muscle fibres, and widely dissociated capillaries lying in a sea of blood. In places there are many leucocytes in the hæmorrhage and to a less extent in the fragments of tissue. The hæmorrhage extends beneath

the decidua throughout the section, affecting rather less than the inner half of the myometrium. It decreases in extent as it passes from the line of cleavage. As it decreases the fibres in the muscular bundles become less and less dissociated, but there is very little diminution in the degeneration and necrosis of the muscle. In the outer half of the myometrium hæmorrhages are absent; the bundles are separated by œdema; there is very little degeneration of muscle fibres and necrosis is confined to some of the more internal bundles.

Section (*h*). *Kidney*. Œdema is indicated by separation of the tubules from one another and from their basement membrane. The cells of the first convoluted tubules and ascending limbs of the loops of Henle vary in size and are frequently ill-defined and vacuolated or fragmented. Numerous nuclei are very faintly stained and shrivelled; pyknotic nuclei are less common; cells without a nucleus are frequent. In many first convoluted tubules the cells are almost completely necrosed. The cells of the second convoluted tubules are fatty and usually dissociated. There are small granules of fat in the epithelium of some of the collecting tubules. In the discharging tubules the cells show perinuclear vacuolation and frequently complete disintegration. There is no cellular infiltration.

Section (*i*). *Liver*. Small sparse fatty granules are present in the hepatic cells and are most numerous in those of the centres of the lobules.

CASE A2. S.D. 1135, 1918 (Case 37 of Appendix, Part I).

MACROSCOPIC EXAMINATION.

A uterus amputated through the upper part of the cervix and hardened in formaldehyde. It measures 15×10×5 cm. The wall is 2 cm. thick at the fundus, and narrows to 1.2 cm. thick at the lower extremity. The peritoneal surface is smooth and pale, save in the following areas. At the lower extremity of the anterior surface is a patch of bright red hæmorrhage (3 cm. diameter) in the subserosa. Around the left cornu the serosa covers a bright red and purple patch (4.5 cm. diameter). On the right cornu is a blue purple area (2 cm. diameter), and a purple area (1 cm. diameter) lies immediately behind the reflection of the right broad ligament near its centre. The inner surface is covered by a velvety, bright red membrane save for an area (12×8 cm.) on the posterior aspect; here the surface is ragged and deep red; this is apparently the placental site. The cut surface here is pure white with scattered, red specks. The cut surface in the upper part of the anterior wall is, in the inner 1.5 cm., bright red and ragged. An incision through the left cornu passes into the placental site. Here on the cut surface there is, immediately beneath the serosa, a layer (0.5 cm. deep) in which white myometrial strands are separated by wide spaces filled by fluid red blood; subjacent to this is a layer (0.8 cm. deep) of white tissue in which are scattered narrow red lines (0.2 cm. long); internal to this is 1 cm. of hæmorrhagic red tissue. An incision through the right cornu shows some narrow clefts, filled with blood, immediately below the serosa; in the remainder of the cut surface, white bundles are separated by bright red lines. In the fundus, in the centre of the right half, the inner two-fifths of the wall are hæmorrhagic and bright red. In other portions of the wall the cut surface shows small grey areas, separated by white bands, and no red areas. Serial transverse sections show scattered red flecks in the wall beneath the placental site. Other parts show scattered red flecks.

Accompanying specimen is a piece of kidney (6×2×2 cm.). Cortex almost white, medulla very pale purple. Labyrinths somewhat opaque and white.

MICROSCOPICAL EXAMINATION.

The following portions were taken for microscopic sections :—(*a*) pure white area in anterior wall of uterus; (*b*) hæmorrhagic area in upper part of anterior wall; (*c*) left cornu (placental site); (*d*) hæmorrhagic area in left cornu; (*e*) kidney. The sections were stained by the same methods as in Case A1.

Section (*a*). *Non-hæmorrhagic anterior wall of uterus.* The decidua consists of a narrow superficial zone of spongy tissue, containing vascular and glandular spaces. There is no cellular degeneration. There is considerable infiltration with lymphocytes and less numerous neutrophil leucocytes, the infiltration being especially periglandular. There are no hæmorrhages and no changes in the walls of the blood spaces.

In a few places in the inner third of the myometrium there are a few red blood cells, immediately outside the vessels. There is widespread but slight perivascular infiltration with lymphocytes, larger mononuclear cells and an occasional neutrophil leucocyte. The infiltration affects the whole wall, but is greatest immediately below the decidua. Certain groups of muscle fibres are narrower than others and are vacuolated. The nuclei in these groups are faintly stained or are absent. These changes are most extensive in the inner quarter. There is intimal proliferation in a few large veins. A section stained with Sudan III shows fine granules of fat filling the cytoplasm of free granule-cells in the fibrous tissue. The muscle cells are free.

Section (*b*). *Hæmorrhagic anterior wall of uterus.* The inner one-sixth is feebly stained and has a homogeneous appearance. No decidua is recognizable. The muscle cells are either shrivelled or swollen, and few contain nuclei. Where the muscle is shrivelled, the interstitial tissue is swollen and is not stained red with van Gieson. There is a little hæmorrhage in this zone. In the subjacent three-sixths there is extensive diffuse hæmorrhage, and also œdematous swelling of trabeculæ (Fig. II). The muscle cells in the inner part of this zone show very similar changes to those just described, but on passing deeper more nuclei are visible, and ultimately there is very little degeneration or necrosis. In the next sixth the muscle bundles are very widely separated by an extreme swelling of the fibrous stroma which is due to impregnation with an albuminous coagulated fluid. The outer sixth appears normal. Leucocytic infiltration is slightly less than in section (*a*). The walls of the arteries and veins in the inner necrotic area are swollen and œdematous; the muscle fibres of the media are shrunken and the majority are without nuclei. Here, and in all other sections, the changes in the walls of the vessels resemble those in the surrounding tissue, but are, if anything, less severe, not more severe. Fat is limited to free cells in the fibrous stroma. Such fatty cells are few, except in the outermost third.

Section (*c*). *Left cornu of uterus, with placental site.* In the inner fifth, which includes a part of the placental site, there is extensive hæmorrhage throughout the spongiosa. This hæmorrhage is, in places, extreme. Where the hæmorrhage is very great, the tissue is entirely destroyed; where great, the decidual cells and, deeper, the muscle fibres, are separated and extensively necrosed. Where the tissue is less dissected by blood,

FIG. II. S. D., 1135/18. Section of myometrium.

Shows (*a*) an extensive haemorrhage; (*b*) degeneration necroses of muscle fibres; (*c*) healthy muscle fibres.

the muscle fibres are less deeply stained and less sharply defined than in the subjacent two-fifths. There is little loss of nuclei. In the next two-fifths hæmorrhage is considerable, but not nearly so extensive as in section (*b*). There is very little evidence of degeneration and necrosis. In nearly the whole of the outer two-fifths there is separation of the muscle bundles by albuminous fluid. This is not seen in the extreme outer part, but here the muscle fibres are feebly stained, ill-defined, often vacuolated and frequently devoid of nuclei. They are less degenerate in the œdematous area. Leucocytic infiltration is greater in the inner two-fifths than in previous sections. In the spongiosa neutrophil leucocytes are numerous and beneath this plasma cells are present in addition to lymphocytes and occasional leucocytes. In the spongiosa the blood spaces are filled by red clot; beneath this zone several arteries are greatly narrowed by intimal proliferation. Fat is again confined to round and spindle connective tissue cells. These cells are most numerous where the myometrium is least altered.

Section (*d*). *Hæmorrhagic left cornu of uterus.* In the outer zone of longitudinal fibres the myometrium appears normal. Internal to this is a broad zone in which muscle bundles are widely separated by hæmorrhage and œdema. Throughout the remainder of the wall are numerous large focal hæmorrhages. Areas of necrosis occupy large portions of the inner third of the wall. Perivascular leucocytic infiltration is less than in previous sections. There are a few fat granule cells in the interstitial tissue.

Section (*e*). *Kidney.* There is a conspicuous cloudy swelling of the epithelium of the first convoluted tubules. In several of these tubules there is severe dropsical degeneration. There is a little cloudy swelling of the epithelium of the ascending loops of Henle. A multinuclear giant cell is seen in the lining of one convoluted tubule. There is slight fatty degeneration of the epithelium of the second convoluted and collecting tubules. Albuminous casts are present in a few ascending limbs of the loops of Henle, and second convoluted, collecting and discharging tubules. The epithelial lining of the tubules in the medulla is separated by œdema. There is no active inflammatory reaction.

Case A3. S.D. 189/19 (Case 41 of Appendix, Part I).

MACROSCOPICAL EXAMINATION.

A uterus amputated through the upper part of the cervix and hardened in Kaiserling No. 1. It measures 17×16×4.5 cm. There is subserous hæmorrhage about both cornua over an area 4 cm. in diameter. Fainter, purple, smaller areas of subserous hæmorrhage are numerous over the posterior surface and there are a few on the anterior surface. On section, the lining of the posterior wall is grey, granular and nodular; on the anterior wall it is rough, ragged and hæmorrhagic. The wall is 2.4 cm. thick in the lower part. There are hæmorrhages in the subserosa which extend for a depth of only 1 cm. into the muscularis. The muscularis elsewhere shows white strands enclosing very small, grey areas and grey, narrow lines. There are also in the muscularis a number of groups, varying in number in different sections, of pin-point, red flecks; they are most numerous in the upper part of the body and much more numerous anteriorly than posteriorly. In the anterior wall of the body near the mucosa are a few ill-defined red areas up to 0.5 cm. in diameter.

NECROPSY.

A complete post mortem examination was performed on this case. The following is an extract of the findings:—*P.M.* 78. 1919. *Anæmia. Operation*: *Hysterectomy for internal accidental hæmorrhage. Toxæmia of pregnancy.* Severe parenchymatous degeneration of liver (14 lbs. 13 ozs.). Numerous faint, pin-head, opaque, yellow necroses throughout liver especially in right lobe. Anæmia of myocardium and of all organs and tissues. Severe parenchymatous degeneration of kidneys (11 ozs.). Slight myeloid transformation of spleen.

MICROSCOPICAL EXAMINATION.

Sections were stained by the methods enumerated above. The following sections were taken from the material obtained by operation: (*a*) from posterior wall of uterus, 2 cm. from lower end, including a few pink points; (*b*) from the right cornu, with hæmorrhage extending for 0.8 cm. beneath serosa; (*c*) from anterior wall, 4 cm. from fundus, to show red area near mucosa.

Section (*a*). *Posterior wall of uterus.* The inner surface is covered by a narrow layer of decidua. In large areas of the inner and central thirds of the myometrium the muscle fibres are vacuolated and ill-defined. Where these changes are greatest the bundles in longitudinal section are represented by an almost homogeneous matrix, composed of indistinct parallel wavy fibrils traversed by parallel ill-defined clefts, and furnished with few nuclei. In cross section such bundles are represented by a meshwork of homogeneous cytoplasm containing a few nuclei and enclosing large vacuolar spaces. There is considerable perivascular infiltration with lymphocytes and larger basophil cells throughout the myometrium, in the decidua there is a similar infiltration in which a few leucocytes are present.

Section (*b*). *Right cornu of uterus.* There is very little muscular degeneration. Infiltration of the myometrium is greater and contains a few leucocytes. The muscle bundles in the outer third of the wall are widely separated by œdema, coagulated albumen and blood. In the outer sixth the bundles appear to float in blood.

Section (*c*). *Anterior wall of uterus.* There are many areas of vacuolar degeneration and necrosis of the muscle in the inner third of the myometrium, and one focal area of necrosis in the central third. In the decidua and inner third of the myometrium hæmorrhages are numerous; in the outer third there are two hæmorrhages and œdema is conspicuous. There is infiltration similar to that in the previous section. There is fat in a few endothelial cells.

The following sections were taken post mortem:—(*d*) from the upper part of the cervix uteri; (*e*), (*f*) and (*g*) from the liver; (*h*) from the kidney, (*i*) from the myocardium, (k) from the diaphragm, (*l*) and (*m*) from the spleen.

Section (*d*). *Upper part of cervix uteri.* There are a few muscular bundles in which the individual fibres have fused so as to form a homogeneous matrix in which nuclei are almost completely absent. More numerous are small areas occupied by a widely meshed net of delicate

collagen fibrils, enclosing large clear spaces. Many of such areas lie within muscular bundles, groups of muscle fibres lying in their periphery and projecting in places into their centtres. They do not, therefore, merely represent œdema of the interstitial tissue, but an œdematous destruction of muscle. Both the above forms of necrosis are found chiefly in the immediate neighbourhood of a large hæmorrhage beneath the mucosa. Isolated areas of œdematous necrosis are found, however, at a distance from the hæmorrhage. In the deeper layers of the muscularis and in the submucosa there is a considerable infiltration which contains many neutrophil leucocytes. In the intermediate muscularis infiltration is very slight, and neutrophil leucocytes are rare.

Sections (*e*), (*f*) and (*g*). *Liver.* There are grey thrombi in a few large hepatic veins. The cells in the outer third of the lobules are small, dissociated, sharply defined and frequently furnished with two nuclei. In the central two-thirds the cells are swollen, arranged in columns, and can seldom be differentiated from one another; many of their nuclei show karyolysis. Large vacuoles lie in the columns chiefly in their periphery.

In sections stained by Sudan III there is much fat in the cells of the central columns; the dissociated peripheral cells seldom contain fat. Proliferation of interstitial tissue and infiltration of portal systems are absent. The capillaries contain many neutrophil leucocytes.

Section (*h*). *Kidney.* The cells of the first convoluted tubules and the ascending limbs of the loops of Henle are swollen, faintly stained and distinctly granular. In many the nuclei are very faintly stained, in others no nucleus is visible. There is a little fat in the cells of the second convoluted tubules and some of the collecting tubules. The cells lining the discharging tubules show extreme perinuclear vacuolation and frequently complete disintegration. There are hyaline casts in several of the discharging tubules.

Section (*i*). *Myocardium.* There is slight œdema of the interstitial tissue. Cross striation is distinct in the muscle fibres. There is lipochrome in the sarcoplasm at the poles of the nuclei, but the fibres contain no fat. There are many leucocytes in the capillaries.

Section (*k*). *Diaphragm.* There is extensive hæmorrhage into the lipomatous tissue beneath the pleura. There are small areas of infiltration with lymphocytes and epithelioid cells in the peritoneal fibrous tissue. Cross striation is distinct in the muscle.

Sections (*l*) and (*m*). *Spleen.* The capillary veins are usually narrow. The reticular strands are somewhat swollen, their fibrils are fragmented, and many of the nuclei of the cells of the reticulum are very faintly stained or are absent. There are very few free cells in the reticular strands. Such as are present are chiefly plasma cells and eosinophil leucocytes.

In the capillary veins and in the peripheral zones of the Malpighian bodies, there are numerous free cells. The great majority of these are neutrophil leucocytes of which many have round nuclei. With these is a considerable number of large mononuclear leucocytes and endothelial cells. Eosinophil leucocytes are relatively rare. There are several neutrophil myelocytes, a few normoblasts and one or two eosinophil myelocytes. No megakarocyte was observed.

GROUP B.

Control Cases.

Case Bi. S.D. 1198. 1918. *Rupture of uterus due to obstructed labour.*

MICROSCOPICAL EXAMINATION.

Section (a). Posterior wall of uterus, above tear. There is considerable patchy infiltration containing many neutrophil leucocytes in the decidua, and very slight perivascular infiltration in the myometrium. There are no hæmorrhages and there is no œdema in the myometrium. The muscle fibres are large and sharply defined (Fig. 3). The only evidence of

Fig. III.

S.D. 1198/18.
Section of myometrium of upper segment showing normal muscular bundles.

degeneration is a vacuolation which is seen in a few fibres, especially in bundles cut transversely. The lumina of the veins and of several arteries are narrowed by a proliferation of the fibrous, elastic and muscular elements of the intima. In sections stained with Sudan III there are a few small granules of fat in a very few spindle and round cells in the interstitial tissue about vessels.

Sections (b) and (c). At right angles to tear in upper uterine segment. In both sections the torn edge is only about one-third the length of the total thickness of the uterine wall, the decidual surface curving outwards

FIG. IV. S. D., 1198/18. Section of stretched lower uterine segments.

Shows (*a*) haemorrhage; (*b*) œdema; (*c*) attenuation of otherwise normal muscle fibres.

towards the line of cleavage. The tear follows the course of large fibrous intermuscular septa, and in (*b*) has opened a large vein. Thus, the uterine wall, before rupture, appears to have thinned at a point where the interstitial tissue was relatively abundant and the muscularis relatively scanty. There is hæmorrhage in the decidua, in intermuscular septa and in the subserosa for a moderate distance from the line of cleavage. In many of the muscular bundles, actually isolated by the hæmorrhage, the fibres are pale and ill-defined whilst their nuclei are shrunken or absent. These bundles are infiltrated with numerous leucocytes. Apart from a slight interstitial œdema the remainder of the myometrium resembles that in section (*a*). In sections stained by Sudan III fat is only found in a very few interstitial cells. The muscular necrosis in these sections is closely associated with the hæmorrhage in the margin of the line of cleavage and appears to be secondary thereto.

Section (d). At right angles to tear in lower uterine segment. The line of cleavage is only slightly shorter than the total depth of the wall, the mucosa curving out for but a short distance. The line of cleavage is remarkably straight. Leucocytic infiltration is present throughout, and is greatest at and near the line of cleavage. There is extreme œdema of the inner three-fifths of the myometrium throughout the section. External to this, the œdema is relatively slight. Extensive hæmorrhages are present throughout and are more abundant towards the limit of the section furthest (2 cm.) from the line of cleavage than in the margin of the line of cleavage. They are most abundant in the inner, extremely œdematous zone. The muscle fibres in the inner three-fifths of the myometrium are widely separated by the œdema and are represented by sinuous threads; loss of nuclei is not appreciable (Fig. 4). In sections stained with Sudan III fat granules are present in a few interstitial cells, and at the poles of the nuclei of some of the attenuated muscle fibres.

The abnormalities in this section are not confined to the margin of the tear nor are they focal in the remainder of the tissue. They are evenly distributed throughout. Compared with the cervix removed post mortem in Case 3 of accidental hæmorrhage (p. 92) the abnormalities are much more general and diffuse. In the case of accidental hæmorrhage there were focal areas of œdema in which the muscle bundles had almost entirely disappeared. In this case there is almost universal dissociation of the muscle fibres by œdema with little evidence of necrosis.

CASE B2 S.D., 732. 1919. *Rupture of uterus in obstructed labour.*

MICROSCOPICAL EXAMINATION.

Section (a). Edge of the laceration in the lower uterine segment. There is hæmorrhage on, in, and in a few places, at a little distance from, the line of fission. The muscle bundles throughout are separated by œdema and there is a little cellular infiltration of the interstitial tissues similar to that in preceding cases. There are a few small hæmorrhagic areas in the decidua at a distance from the line of cleavage. The fibres of the myometrium appear almost without exception to be longer and more sharply defined than in the previous case. Within the areas of hæmorrhage the fibres, in some of the bundles, are ill-defined and are occasionally slightly vacuolated. There appears also to be some loss of nuclei. Nowhere, however, are there the conspicuous degenerations and necroses

which were widely distributed throughout the myometrium in the cases of accidental hæmorrhage.

Section (b). Edge of laceration in dilated lower uterine segment. The line of cleavage is less than two-thirds of the depth of the uterine wall, the decidua and subjacent myometrium curving out towards the line of cleavage. At, and for some distance from, the edge of the laceration hæmorrhages are numerous through the myometrium. In the subserosa great hæmorrhage extends for a long distance from the edge of the rupture. There are very numerous hæmorrhages in the submucosa and subjacent myometrium to a depth rather less than the inner half of the wall. External to this there are scattered small hæmorrhagic areas. There is great œdema throughout. Perivascular infiltration, containing many neutrophil leucocytes is also present throughout. For a considerable distance from the edge of the rupture the muscle fibres are represented by widely separated, very narrow, often sinuous fibrils containing spindle nuclei. Throughout the remainder of the wall the muscularis has for the greater part undergone a similar change. Bundles of stout fibres are present, however, in the outer half of the wall, and occasional bundles showing only slight dissociation are present at the sides of some of the larger vessels. In the more solid bundles a considerable number of the fibres have undergone hyaline degeneration and there is a deficiency of nuclei. The changes in the cervix resemble those in Case B1, and differ in the same manner from those in the cervix in Case A3 of accidental hæmorrhage.

CASE B3. S.D., 1277b. 1919. *Placenta prævia and intra-uterine hæmorrhage.*

MICROSCOPICAL EXAMINATION.

Section of wall of upper uterine segment. There is considerable infiltration of the decidua; among the infiltrating cells is a moderate number of leucocytes. In the remainder of the wall there is a slight perivascular infiltration in which leucocytes are scanty. Compared with the cases of accidental hæmorrhage the muscle fibres are stout and show very little variation in size and, with the exception of a narrow zone immediately beneath the mucosa, they are much more sharply differentiated. A vacuolar degeneration of different type is present. In the transversely cut bundles of the subserous zone perinuclear vacuolation is very conspicuous; many bundles appear to be almost entirely composed of a mosaic of rounded spaces containing central nuclei. Occasional fibres showing a similar vacuolation, but usually of less degree, are seen throughout the rest of the myometrium.

CASE B4. S.D., 1419. 1917. *Rupture of uterus; slight obstruction; albuminuria.*

MICROSCOPICAL EXAMINATION.

Sections (a) and (b). Placental site on anterior wall of uterus. Vacuolation, loss of definition, and loss of nuclei is very widely spread throughout the inner half of the myometrium. They are less in degree and distribution in the outer half. There are no hæmorrhages. There is considerable œdema of the outer half of the myometrium. In sections stained by Sudan III there are fat granules in a very few interstitial cells in the outer half of the myometrium.

Sections (*c*) and (*d*). *Posterior wall of uterus.* Resemble sections (*a*) and (*b*) save that in the outer longitudinal layer the muscle fibres are shrunken and vacuolated.

Section (*e*). *Lower uterine segment at right angles to serous and subserous prolongation of tear.* The uterine wall tapers towards the lower or cervical end. Vacuolation and loss of differentiation of the muscle fibres is present throughout the inner half of the myometrium. In the outer half, in the margins of the tear, the bundles are isolated by hæmorrhage; the fibres show similar changes, or are hyaline, and there is extensive loss of nuclei. On both sides of the tear there is great œdema of the outer half of the myometrium. On the uterine side the muscular bundles are separated by the œdema and there is conspicuous karyolysis. On the cervical side the fibres in the bundles are dissociated and are seen as sinuous threads usually furnished with nuclei. On this side there are hæmorrhage and great infiltration with leucocytes. In sections stained with Sudan III fat is present not only in interstitial cells but at the poles of the nuclei of a few attenuated muscle fibres.

CASE B5. S.D., 930. 1919. *Rupture of uterus produced by manual dilatation of cervix.*

MICROSCOPICAL EXAMINATION.

Section (*a*). *Uterine wall at placental site.* There is a slight dissociation of the muscle fibres such as occurs when specimens have been kept for some time before fixation. The muscle fibres in the inner sixth of the myometrium are less deeply stained, and in general slightly smaller than those in the outer five-sixths. In this inner zone the fibres in longitudinal section are frequently split by narrow longitudinal clefts, and the individual fibres cannot be differentiated. There are no hæmorrhages. There is an infiltration similar to that in all previous cases.

In sections stained with Sudan III granules of fat are present in a considerable number of cells of the interstitial tissue, chiefly in spindle cells.

Section (*b*). *Uterine wall opposite placental site.* In the inner quarter of the myometrium the fibres show a slightly greater degree of the degeneration present in the inner sixth of section (*a*). In a few fibres the nuclei are shrunken, or are only just recognizable; a few fibres are without nuclei.

SUMMARY AND COMPARISON OF MICROSCOPIC FINDINGS.

In the uterine wall of the three cases of accidental hæmorrhage the following histological changes were found:—An infiltration of the decidua with cells among which neutrophil leucocytes were numerous; a slight perivascular infiltration of the myometrium, which decreased in amount from within outwards, and in which leucocytes were scanty; a conspcuous leucocytic infiltration in the margins of the rupture (Case A1); fat granules in occasional interstitial cells and endothelial cells, and, in A1, apparently also in degenerate muscle fibres; a conspicuous œdema, usually albuminous, in the outer part of the myometrium; widespread, conspicuous, focal areas of degeneration and necrosis in the myometrium of the upper uterine segment, especially in its inner half;

widely-spread areas of hæmorrhage in the myometrium of the upper uterine segment; an absence of invariable coincidence between the areas of necrosis and of hæmorrhage, so that the necrosis could not be considered to be secondary to the hæmorrhage; in A3 in which examination was made of the lower uterine segment, a large focal area of necrosis, hæmorrhage and œdema in the inner portion of the myometrium.

In the uterine wall of the five cases taken as controls the following changes which had been found in the three cases of accidental hæmorrhage were again found in all cases; the cellular infiltration of the decidua and myometrium; the conspicuous leucocytic infiltration in the margins of ruptures; fat granules in occasional interstitial cells and endothelial cells, throughout the myometrium.

In B1, a case of rupture of the uterus in obstructed labour, and in B4, rupture of the uterus following trivial obstruction to labour, fatty granules were also found at the poles of the nuclei of a few muscle fibres in the neighbourhood of the ruptures.

In other respects the control cases differed from those of accidental hæmorrhage: œdema in the upper uterine segment of the control cases was confined to the neighbourhood of ruptures; but was found throughout such sections as were taken of the stretched lower uterine segment (Cases B1, B2, rupture of uterus due to obstruction, and B4, rupture of uterus associated with trivial obstruction).

In B1, a case of rupture of the uterus due to obstructed labour, necrosis was confined to muscle fibres enclosed within the hæmorrhage at the margin of the rupture. The muscle fibres in the lower uterine segment were greatly elongated and attentuated, but necrosis was not observed. In the upper uterine segment, the margin of the rupture being excluded, the only evidence of degeneration was vacuolation of a few muscular fibres. In B2, the second case of rupture due to obstruction, sections were taken from the lower uterine segment alone, including the rupture. There were, again, degeneration and some necrosis of fibres included within areas of hæmorrhage, and great elongation and attentuation of the muscle fibres throughout. In B3, the case of distension of the uterus by hæmorrhage due to a placenta prævia, the upper uterine segment was alone examined; degeneration was confined to a perinuclear vacuolation of the fibres in the longitudinal layer of muscle beneath the serosa. In B4 the case of rupture of the uterus with trivial, obstruction, widely-spread degeneration and necrosis of the muscle were present in the inner half of the myometrium of the upper and lower segments. This necrosis was less severe than in the cases of accidental hæmorrhage. In the lower segment there was also the attenuation of muscle fibres seen in B1 and B2. In B5, the case of rupture of the uterus during manual dilatation of

the cervix, degeneration and necrosis were again present in the inner portion of the myometrium in both portions of the upper segment examined. The necrosis was less severe than in B4.

Hæmorrhage in the upper uterine segments of the control cases was confined to the margin of a rupture (B1). In the lower uterine segment hæmorrhage was found in the margin of ruptures (Cases B1, B2 and B4) and a diffuse hæmorrhage was also found in the two cases in which the rupture was due to gross obstruction (B1 and B2).

Where in the upper segment of the control cases there were both hæmorrhages and necroses, the necroses were found within areas of hæmorrhage at the margins of ruptures; the necrosis appeared to be the result of isolation of muscular bundles by hæmorrhage.

Comparison of the cases of accidental hæmorrhage (A) with the control cases (B) shows, therefore, that certain changes were present in all the uteri examined. These changes were: infiltration of the decidua with cells among which neutrophil leucocytes were numerous, a perivascular infiltration throughout the myometrium which decreased in amount from within outwards and in which leucocytes were scanty; fat granules in a few cells of the interstitial tissue, in a few endothelial cells and in a very few muscular fibres.

Inasmuch as these changes were present not only in the cases of accidental hæmorrhage but in all the examples of various conditions taken as controls, they appear to be changes common to all uteri about full time. They are certainly not peculiar to cases of accidental hæmorrhage.

Further, hæmorrhage and a conspicuous leucocytic infiltration were present in the margins of all ruptures, not only in the case of accidental hæmorrhage but in the control cases.

This hæmorrhage and leucocytic infiltration can only be considered to be the result of rupture.

In the cases of accidental hæmorrhage focal hæmorrhage was widespread throughout the myometrium of the upper uterine segment. In the control cases there was no hæmorrhage in the myometrium of the upper uterine segment, except in the margins of ruptures. In the lower uterine segment, however, of two of the control cases (B1 and B2) diffuse hæmorrhage was associated with attenuation and elongation of the muscular fibres. The two control cases were cases of rupture of the uterus due to obstruction to labour.

Diffuse hæmorrhage was found, therefore, in the stretched, lower uterine segment of the two cases of obstruction to labour. There can be little doubt that these hæmorrhages were the direct result of mechanical stretching of the lower uterine segment. The upper segment of these uteri was doubtless protected from stretching and

consequent hæmorrhage by active contraction and retraction. These observations suggest that the hæmorrhages in the upper segment of the three cases of accidental hæmorrhage may have been due to stretching, by internal hæmorrhage, of upper segments which were not protected by active contraction. This conclusion is excluded, however, first by the absence of microscopic evidence of stretching of the muscular fibres, and secondly by the control case B3. In Case B3 there was, owing to separation of a placenta prævia during the bringing down of a leg, a greater distension of the uterus, by internal hæmorrhage, than in any of the cases of accidental hæmorrhage. Further, contraction and retraction of the upper segment in this case were excluded, the uterus being in a state of atony produced by chloroform. Yet, in this case, B3, there was no hæmorrhage in the upper uterine segment.

It can be concluded, therefore, that diffuse hæmorrhage in the lower segment of the cases of obstructed labour was due to mechanical stretching, but the widespread hæmorrhage in the upper uterine segment of the cases of accidental hæmorrhage cannot be ascribed to a similar mechanical cause.

For similar reasons the great œdema, for the most part albuminous, which was present in the outer zones of the myometrium throughout the uteri in the cases of accidental hæmorrhage cannot be ascribed to mechanical stretching, although great œdema was present in the stretched lower segment of the control Cases B1 and B2 in which the uterus ruptured owing to definite obstruction to labour, and B4 in which the uterus ruptured in the presence of trivial obstruction to labour. Neither can the œdema found in the cases of accidental hæmorrhage be considered of similar origin to that found in the upper uterine segment of control cases. In the control cases it was only found in the margins of ruptures; in the cases of accidental hæmorrhage it was present in all sections, including those of the two cases in which there was no rupture.

The following changes were, therefore, peculiar to the cases of accidental hæmorrhage:—a severe œdema and a widespread focal hæmorrhage in the myometrium which were independent of stretching and of rupture.

Finally, in all three cases of accidental hæmorrhage, focal areas of degeneration and necrosis were widespread throughout the myometrium, especially in the inner zones. This degeneration and necrosis were associated with hæmorrhage, but they were not due to the hæmorrhages because they did not occur invariably in areas in which hæmorrhage was present. They differed, therefore, from the degeneration and necrosis found in control cases within the hæmorrhages at the borders of ruptures. The degenerations and necroses were even more conspicuous than the widespread hæmorrhage and œdema which have been shown to be peculiar to the

cases of accidental hæmorrhage. But these degenerations and necroses were not peculiar to the cases of accidental hæmorrhage. They were found in less degree in Case B4, in which rupture of the uterus was associated with trivial obstruction, and in still less degree in Case B5, in which the uterus ruptured during manual dilatation. On the other hand, they were not found in the two cases of rupture due to obstructed labour (B1 and B2) nor in the case of distension of the uterus by hæmorrhage in placenta prævia (B3).

From comparison of the conditions within all the uteri examined and of the mechanical conditions to which these uteri were exposed, it is not possible to find an explanation of the incidence of these necroses. An explanation may be found when other features in the cases are taken into consideration.

In all three cases of accidental hæmorrhage, toxæmia was indicated by the presence of albuminuria during life, and was proved by such histological examinations of the kidney and liver as were made; that is of the kidney in all three cases and of the liver in two cases. In the kidneys there was a severe albuminous and a slight fatty degeneration. In one liver there was a conspicuous fatty degeneration; in the other there was fatty degeneration in the centres of the lobules, whilst in the periphery of the lobules there were changes indicative of a slow destruction and regeneration of parenchyma.

In the control Case B4 there was also evidence of a toxæmia of pregnancy; a severe albuminuria was present, and disappeared soon after the removal of the ovum and uterus.

In the absence of any other explanation of the degeneration and necrosis in the myometrium of the three cases of accidental hæmorrhage and of Case B4, the fact that they were associated with a toxic degeneration of other organs leaves little doubt that the changes in the myometrium were the result of a toxæmia of pregnancy. The absence of evidence of toxic degeneration of the kidney as shown by albuminuria, in Case B5 does not nullify this conclusion. The degeneration and necrosis in Case B5 were of less degree than in the other four cases. They may well have been due to a toxæmia of slighter intensity.

The degeneration and necrosis of the myometrium evidently rendered the uterus liable to rupture. In one of the three cases of accidental hæmorrhage, the uterus ruptured in the absence of any abnormal obstruction to labour. In Case B4 the uterus ruptured in the presence of an obstruction insufficient to cause rupture of a normal uterus. It is possible that the uterus in Case B5 ruptured under a strain which a normal uterus would have withstood; unfortunately no information could be obtained concerning the strain to which the uterus was subjected by the manual dilatation.

Name.	Age.	Parity.	Degree of Albuminuria.	Toxæmic Symptoms.	Period of Gestation.	Abdominal Pain.
1. M.K.	36	VIII. Ch. 8, misc. 0	—	—	31½ weeks	—
2. E.B.	21	0	In quantity	?	?	?
3. L.K.	28	III. Ch. 3, misc. 0	In quantity	?	?	?
4. A.A.	33	IV. Ch. 3, misc. 1	4/1,000 (Esbach), hyaline and granular casts	—	Term	Present
5. F.J.	28	III. Ch. 3, misc. 0	—	—	Term	—
6. M.W.	33	V. Ch. 4, misc. 1	In quantity	—	34 weeks	Present
7. A.N.	32	II. Ch. 2, misc. 0	Fine cloud	—	Term	—
8. F.W.	19	0	In quantity, no casts	—	32 weeks	Present
9. C.P.	43	XII. Ch. 12, misc. 0	—	—	38 weeks	—
10. L.S.	34	III. Ch.2, misc. 1	In quantity	—	29 weeks	—
11. A.H.	40	VIII Ch. 8, misc. 0	?	Swelling of feet and legs 5 weeks	Term	—
12. A.S.	25	I. Ch. 1, misc. 0	In quantity	Swelling of legs and hands 3 weeks	Term	Present at 30th week
13. G.M.	29	II. Ch. 2, misc. 0	In quantity	—	37 weeks	—
14. J.F.	24	0	In quantity	Swelling of legs, face and abdominal wall 14 days, headache and excitability during labour	37 weeks	—
15. E.H.	42	XI. Ch. 9, misc. 2	In quantity	—	38 weeks	Present
16. L.R.	31	V. Ch. 3, misc. 2	1.8/1,000 (Esbach)	Swelling of legs, feet and face 4 weeks	33½ weeks	Present
17. M.S.	42	VII. Ch. 7, misc. 0	3/1,000 (Esbach), granular casts	—	36 weeks	—
18. R.S.	39	IX. Ch. 7, misc. 2	0.75/1,0000 (Esbach), no casts	—	38 weeks	—
19. A.H.	36	XII. Ch. 11, misc. 1	Fine cloud	—	38 weeks	—
20. B.C.	34	I. Ch. 1, misc. 0	Fine cloud, granular casts	—	31 weeks	Present
21. M.S.	19	0	Fine cloud	—	?	—
22. A.J.	32	III. Ch. 2, misc. 1	In quantity	Headache 1 month	?	Present
23. P.R.	26	I. Ch. 1, misc. 0	Fine cloud	—	38 weeks	Present
24. E.B.	24	II. Ch. 2, misc. 0	2/1,000 (Esbach), hyaline and granular casts	—	35 weeks	Present
25. E.D.	25	III. Ch. 3, misc. 0	Thin cloud, no casts	Swelling of legs 3 weeks, headache throughout	Term	—
26. S.L.	38	IV. Ch. 4, misc. 0	—	—	37 weeks	—
27. L.J.	41	IX. Ch. 9, misc. 0	In quantity, granular casts	—	Term	Present
28. E.C.	39	IX. Ch. 8, misc. 1	Fine cloud	—	35 weeks	Present
29. E.D.	30	I. Ch. 1, Misc. 0	In quantity, no casts	—	38½ weeks	Present

Period of gestation	Abdominal Pain.	Type.	Day of puerperium on which urine became free from albumen.	Treatment.	Result. Mother.	Child.
1½ weeks	—	External	—	Membranes ruptured, leg brought down	G.	D.
?	?	Combined, internal>external	—	Forceps delivery, pituitrin	D.	S.B.
?	?	Internal	10th day	Cæsarean section	G.	S.B.
Term	Present	Internal	17th day	Cæsarean section	G.	S.B
Term	—	External	—	None	G.	G.
4 weeks	Present	Combined, int.>ext.	9th day	Membranes ruptured, vagina plugged, pituitrin	G.	S.B.
Term	—	Retro-placental hæmatoma	14th day	None	G.	G.
2 weeks	Present	Combined, int.>ext.	4th day	Membranes ruptured, vagina plugged, pituitrin	G.	S.B.
8 weeks	—	External	—	External ver-ion. membranes ruptured foot brought down	G.	D.
29 weeks	—	External	4th day	None	G.	S.B.
Term	—	Combined, int.>ext.	—	None	G.	S.B.
Term	Present at 30th week	Retro-placental hæmatoma at 26th and 30th week	Chronic nephritis	None	G.	G.
37 weeks	—	Combined, ext.>int.	13th day	None	G.	G.
37 weeks	—	Internal	9th week	None	G.	S.B.
38 weeks	Present	Combined, int.>ext.	11th day	Membranes ruptured, vagina plugged, pituitrin	G.	S.B.
33½ weeks	Present	Combined, int.>ext.	7th day	Membranes ruptured, vagina plugged, pituitrin	G.	S.B.
36 weeks	—	Combined, int.>ext.	8th day	None	G.	S.B.
38 weeks	—	Internal	10th day	None	G.	S.B.
38 weeks	—	Combined, ext.>int.	13th day	Membranes ruptured, tight binder	G.	S.B.
31 weeks	Present	Combined, int.>ext.	9th day	None	G.	S.B.
?	—	Internal	8th day	None	G.	S.B.
?	Present	Combined, int.>ext.	6th day	Pituitrin	G.	S.B.
38 weeks	Present	Combined, int.>ext.	3rd day	Membranes ruptured, vagina plugged, pituitrin	G.	S.B.
35 weeks	Present	Combined, int.>ext.	10th day	Membranes ruptured, vagina plugged, pituitrin	G.	S.B.
Term	—	Internal	6th day	None	G.	S.B.
37 weeks	—	Combined, ext.>int.	—	Pituitrin, tight binder	G.	S.B.
Term	Present	Combined, int.>ext.	—	Membranes ruptured, vagina plugged, pituitrin, rupture of uterus, hysterectomy	D.	S.B.
35 weeks	Present	Combined, int.>ext.	4th day	Membranes ruptured, tight binder, pituitrin	G.	S.B.
38½ weeks	Present	Combined, int.>ext.	6th day	None	G.	S.B.

Name. Age.	Parity.	Degree of Albuminuria.	Toxæmic Symptoms.	Period of Gestation.	Abdominal Pain.
30. R.O. 31	IV. Ch. 2, misc. 2: 1st misc., 2nd 6/12 mac., 3rd misc., 4th 8/12 mac.	Fine cloud	General malaise	23 weeks	—
31. M.B. 42	XIII. Ch. 12, misc. 1	Fine cloud	—	31 weeks	Present
32. G.C. 21	0	Fine cloud, granular casts	Vomiting 14 days, jaundice post-partum	34 weeks	—
33. R.P. 32	VI. Ch. 5, misc. 1	6/1,000 (Esbach), no casts	Swelling of legs 2 days	Term	Present
34. S.K. 24	0	2/1,000 (Esbach), hyaline and granular casts	Swelling of face 19 days, legs 7 days, headache and vomiting throughout pregnancy	31 weeks	Present
35. L.H. 39	VIII. Ch. 8, misc. 0	1/1,000 Esbach	Swelling of legs 3 weeks	28 weeks	Present
36. K.W. 29	0	In quantity	—	38 weeks	—
37. J.F. 40	XIII. Ch. 12, misc. 1	4/1,000 (Esbach), hyaline and granular casts	—	32 weeks	Present
38. A.C. 32	IX. Ch. 10, twins (2), misc. 1.	2/1,000 (Esbach), hyaline and granular casts	—	33½ weeks	—
39. A.H. 32	IV. 1st, 2nd and 3rd 36 weeks mac., 4th 36 weeks induction	Fine cloud	Headache and vomiting throughout	24 weeks	—
40. S.S. 29	VIII. Ch. 6, misc. 2	—	—	37 weeks	—
41. C.W. 37	VII. Ch. 7, misc. 0	12/1,000 (Esbach), hyaline and granular casts	Headache 2 days	Term	Present
42. M.E. 28	V. Ch. 4, misc. 1: 1st misc. 5/12, 2nd S.B. 8/12, 3rd term, alive, 4th S.B. 7/12, 5th term, alive	6/1,000 (Esbach), hyaline and granular casts	Headache 1 day ante-partum, persistent vomiting, headache and drowsiness for 48 hours post-partum	35 weeks	—
43. E.H. 35	IX. Ch. 8, misc. 1	Cloud, hyaline and granular casts	Headache 1 month	38 weeks	Present
44. E.R. 28	II. Ch. 2, misc. 0	Fine cloud	—	34 weeks	—
45. E.G. 29	I. Ch. 1, misc. 0	—	—	Term	—
46. S.K. 27	II. Ch. 2, misc. 0	—	—	34 weeks	—
47. E.E. 34	III. Ch. 3, misc. 0	0.5/1,000 (Esbach)	—	32 weeks	—
48. C.W. 39	XV. Ch. 13, misc. 0	1/1,000 (Esbach), granular casts	—	38 weeks	—
49. I.Y. 21	0	Fine cloud, pus cells, colon bacilli	Pyelitis of pregnancy, swelling of legs 1 month	Term	Present
50. L.C. 29	0	15/1,000 (Esbach)	Eclampsia.	34 weeks	—

Vomiting occurred in Nos. 4, 6, 8, 12, 15, 23, 24, 27, 28, 29, 31, 33, 34, 37, 38, 41, 42, 43, 44, 50.

There was pronounced anæmia in Nos. 2, 3, 4, 6, 8, 9, 15, 16, 19, 22, 23, 24, 26, 27, 28, 29, 31, 33, 34, 35, 36, 37, 38, 41, 42, 43, 47, 48.

Fainting occurred in Nos. 2, 3, 4, 6, 15, 27, 28, 31, 33, 34, 35, 36, 37, 41, 42, 43, 47.

Period of Gestation	Abdominal Pain.	Type.	Day of puerperium on which urine became free from albumen.	Treatment.	Result. Mother.	Result. Child.
23 weeks	—	Retro-placental hæmatoma	Chronic nephritis	None	G.	S.B.
31 weeks	present	Combined, ext.>int.	5th day	Membranes ruptured, vagina plugged, pituitrin	G.	S.B.
34 weeks	—	External	5th day	Membranes ruptured, pituitrin	G.	S.B.
Term	present	Internal	4th day	Cæsarean section	G.	S.B.
31 weeks	present	Retro-placental hæmatoma	10th week	None	G.	S.B.
28 weeks	present	Internal	7th day	None	G.	S.B.
38 weeks	—	Combined, int.>ext.	4th day	None	G.	S.B.
32 weeks	present	Internal	—	Cæsarean section, hysterectomy	D.	S.B.
33½ weeks	—	Combined, ext.>int.	8th day	Membranes ruptured, foot brought down, pituitrin	G.	S.B.
24 weeks	—	Retro-placental hæmatoma	Chronic nephritis	None	G.	S.B.
37 weeks	—	External	—	None	G.	G.
Term	present	Internal	—	Cæsarean section, hysterectomy	D.	S.B.
35 weeks	—	Combined, int.>ext.	Trace 14th day	Membranes ruptured, tight binder	G.	S.B.
38 weeks	present	Internal	10th day	Watched, later membranes ruptured, tight binder, pituitrin	G.	S.B.
34 weeks	—	Combined, ext.>int.	2nd day	Membranes ruptured, tight binder, pituitrin	G.	S.B.
Term	—	External	—	None	G.	G.
34 weeks	—	Combined, ext.>int.	—	None	G.	S.B.
32 weeks	—	Combined, ext.>int.	—	None	G.	G.
38 weeks	—	Combined, ext.>int.	6th day	None	G.	G.
Term	present	Retro-placental hæmatoma	2nd day	None	G	G.
34 weeks	—	Retro-placental hæmatoma	6 months	Cæsarean section for eclampsia	G.	G.

Placental infarcts were found in Nos. 11, 12, 14, 16, 17, 23, 25, 30, 34, 39, 43, 44, 49, 50.
The umbilical cord measured 20 inches or more in length in all but nine cases, viz., 13 ins. in No. 44; 14 ins. in No. 34; 16 ins. in No. 1; 17 ins. in No. 9; 18 ins. in Nos. 6, 10, 18, 30; and 19 ins. in No. 14.
The Wassermann reaction was tested in 15 cases and was found positive in one only—No. 42.

Conclusions.

1. The changes characteristic of, and peculiar to, cases of accidental hæmorrhage are widespread necrosis, hæmorrhage and œdema in the myometrium.

2. These changes are not due to mechanical injury.

3. The necrosis is closely associated with the hæmorrhages but is not due to the hæmorrhages. The necrosis, hæmorrhage and œdema are due to the same cause.

4. The cause is a toxæmia of pregnancy, which damages the kidneys and liver as well as the uterus.

5. A less degree of this toxæmia can cause necrosis of the myometrium without hæmorrhage and œdema (Case B4).

6. A still less degree can cause a slight degree of necrosis without hæmorrhage and œdema, and without an albuminuria giving evidence of poisoning of the kidney (Case B5).

7. The necrosis of the myometrium renders the uterus liable to rupture.

8. In the uteri affected by this necrosis evidence of fatty degeneration is extremely slight, and is no greater than that in normal uteri at full time.

To Professor Hubert M. Turnbull, I am greatly indebted for kindly encouragement, assistance and criticism. His help has been invaluable. The work has been arduous and has required much critical investigation and careful controlling on his part. Nevertheless I have always found him more than willing to devote his time and mind thereto.

To Mr. J. R. Ford my thanks are due for his careful and excellent illustrations.

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The Accouchement of Queen Jane Seymour.

By S. D. Clippingdale, M.D. (Aberdeen), F.R.C.S. (Eng.).

(1) Historic Note upon Cæsarian Section.

Cæsarian section, in this country, prior to the introduction of antiseptic surgery, seems to have been peculiarly fatal to the mother. Ramsbotham,[1] writing in 1841, states that he was acquainted with only thirty cases of the operation, and that in only three of these had the mother recovered. Abroad, the operation seems to have been attended with greater success.

The operation is an ancient one. Pliny [2] mentions it, and says Scipio Africanus (B.C. 237) was born in this way. As is well known, the procedure takes its name from the fact that Julius Cæsar is reputed to have been born in this manner. If this was so, Cæsar's mother must have survived the operation, for she was living when her son invaded Britain (B.C. 55).

The earliest medical writer upon Cæsarian section was Guy de Cauliac,[3] who, however, only advocated the operation for the purpose of delivering a living child from a dead mother. De Cauliac published his work in 1363. In 1581 Russett [4] wrote advocating the operation during the mother's lifetime. Russett's work seems to have given a considerable stimulus to the operation which was soon practised with considerable success in many parts of the Continent. Instances are recorded in which the operation was practised more than once upon the same woman, the most remarkable case of this kind being, perhaps, that in which a surgeon of Bruges delivered his own wife by this method no fewer than seven times.[5]

Among the traditional cases it may be mentioned that Æsculapius, the God of Physic is said to have been thus born (Ovid), and, according to Shakespeare, Macduff was "from his mother's womb untimely ripp'd."[6]

(2) The Case of Queen Jane.

Henry VIII at the time he married Lady Jane Seymour had had but two Queens—Katharine of Arragon, who had borne the Princess (afterwards Queen) Mary, and Anne Boleyn, who had

borne the Princess (afterwards Queen) Elizabeth. Neither Queen had borne a son to live.

Lady Jane Seymour was a woman of noble parentage and of ancient lineage. Her father, Sir John Seymour, in attendance upon the King when he visited Francis I in France, and when he received the Emperor Charles V in this country, was descended from the ancient Lords of St. Maur in Normandy. Her mother was a daughter of Sir Henry Wentworth, of Nettlestead, Suffolk. Of this union, Lady Jane was the eldest of eight children. The King, to celebrate his marriage with Lady Jane (her father dying shortly after it) conferred peerages upon her two brothers then living; the elder became Viscount Beauchamp, and the younger Baron Seymour of Sudeley.

Lady Jane Seymour entered the service of Queen Anne Boleyn as Maid of Honour, but at what time is not known. Seeing, however, that the unfortunate Queen Anne had a reign of only three years it could not have been long either after her coronation or before her death. It was, however, sufficiently long for the King to be attracted by her. The King always took a special interest in the Maids of Honour of his Queens, so that it is not surprising to learn that during Queen Anne's lifetime he sent Lady Jane Seymour, then residing at Greenwich, a purse of sovereigns with a note containing amorous proposals. Lady Jane returned the letter unopened together with the purse, accompanied by a message that "her honour was her fortune."[7] The attention which the King paid the Maid of Honour much distressed the Queen, and is said to have caused a miscarriage in January 1536.

The King beheaded the Queen May 19, 1536, and, without spending unnecessary time in unavailing reflection, straightway married Lady Jane, married her in fact on the following day. For the festivities of this marriage, the cakes must have been baking, as pointed out by Miss Strickland,[8] the previous day.

The age of Lady Jane when she married the King is not exactly known. Authorities agree that she was about twenty-eight. She must therefore have been approaching her thirtieth year when, seventeen months later, her confinement occurred. This momentous event took place near midnight on Friday, October 12, 1537, at Hampton Court Palace. That she did not become *enciente* soon after marriage is proved by the fact that when, in July 1536, the question was raised in Parliament as to the succession, answer was returned that the matter might be allowed to stand over as there was no prospect of the Queen becoming a mother.

The question as to whether Queen Jane was delivered by the Cæsarian section will probably never be definitely settled. Material evidence would depend upon the date of her death. If this had

taken place a day or two after her accouchément, Cæsarian section would probably be indicated, but if death did not occur for twelve days some other cause needed finding. The youthful King Edward himself, in the diary which he kept, informs us that his mother died a "few days" after his birth, and Sanders, the priest, in his *De Originæ et Progressus Schismatici Anglicanæ* (1585) states that the Queen's death took place upon the second day. This mistake, for such it undoubtedly is, has been reproduced by other writers, and even occurs in the current issue of Burke's *Peerage*; concerning which the writer addressed a letter to the Editor, and received the following reply, admitting the error:—

> "On reference to the records of Heralds College, I find that "Jane Seymour, third Queen of Henry VIII, died on the "24th October, 1537, and was buried on the 14th November. "This is good evidence as the funeral arrangements were in "the hands of the Heralds. Thanking you for drawing my "attention to the point,
>
> "Believe me,
>
> "Yours faithfully,
>
> "ASHWORTH P. BURKE, Editor."

Details of the confinement, scanty though they are, are given by Miss Strickland and in the *Dict. Nat. Biog.* In accordance with the Court etiquette of the time, Queen Jane had to keep her room for a month before the date of her expected confinement. This deprivation of fresh air and exercise would not conduce to a satisfactory delivery. Four days after delivery it was necessary for the infant Prince to be taken into the chapel of Hampton Court Palace to be baptised. His mother accompanied him, being carried upon a litter. The King, who seems to have had a genuine affection for the Queen, sat by her side, holding her hand. There is no evidence that the Queen took special harm by this early removal from her lying-in chamber. That she, however, became seriously ill later seems shown by the fact that the King intended to have gone to Esher, but remained at Hampton on account of the Queen's altered condition. Early upon the day of her death the doctors reported to the Privy Council as follows:—

> "These shall be to advise your Lordships of the Queen's "estate. Yesterday afternoon she had a natural lax by reason "whereof she began to lighten and (as it appeared) to amend, "and so continued till towards night. All this night she hath "been very sick and doth rather appare than amend. Her "Confessor hath been with Her Grace this morning, and hath

" done what to his office appertaineth and even now is prepar-
" ing to Her Grace the Sacrament of unction.
" At Hampton Court this Wednesday morning at
eight a clock.

" Your Lordships at Commandment.
" THOMAS CUTLAND. JOHN CHAMBERS, Priest.
" ROBERT KARHOLD. WILLIAM BUTTS.
" EDWARD BAYNTAM. GEORGE OWEN."[9]

Of the six doctors who sign this certificate, the first three appear to have been apothecaries, the rest—Chambers, Butts and Owen—were Court Physicians. Chambers was in Holy Orders.

With a view of ascertaining whether the Seymour family possessed any evidence of the alleged Cæsarian section, the writer applied to the present head of the family, His Grace the Duke of Somerset, and was favoured with the following reply :—

" 35, Grosvenor Square, W., 30/5/16.
" Dear Sir,—In reply to yours of yesterday, I regret to say
" that though I have Queen Jane Seymour's marriage settle-
" ment, I have no record as to the cause of her death.
" I remain, yours faithfully, SOMERSET."

There appears to be ample authority for the rumour, supported by Miss Strickland, that when the doctors, owing to the protraction of the Queen's labour, explained to the King that an operation (apparently either craniotomy or Cæsarian section) would be necessary to terminate the labour and requesting His Majesty's direction in the matter, the King replied, " Save the life of the child for another wife can easily be found."*

The period of gestation at which the confinement took place appears to have been normal. The Queen rode horseback across the frozen Thames in January ; the announcement of her being with child was made in March, and her confinement took place in October.

Whether the confinement was natural or artificial the Queen was able to write, or dictate and sign, two days later the following letter to the Privy Council :—

" Right truly and well beloved we greet you well and foras-
" much by the inestimable goodness and grace of Almighty

* An exactly opposite reply was made by the Emperor Napoleon (in the case of his consort), who when appealed to by the doctors replied, " Treat the Empress as you would the wife of a tradesman in the Rue St. Denis. Save both lives if you can, but if you cannot save both lives, save the life of the Empress."

"God we be delivered and brought in childbed of a PRINCE
"conceived in most lawful Majesty between My Lord the
"King's Majestie and Us. Doubting not but for the Love and
"Affection which you bear unto Us and the Commonwealth
"of this Realm this Knowledge shall be joyous and glad
"tidings unto you, We have thought good to certifie of this
"same, to the intent ye might not only under God condign
"thanks and praise for so great a benefit but also continually
"pray for the long continuance and preservation of the same
"here in this life, to the honour of God, joy and pleasure of
"my lord the KING and Us and the universal weal, quiet and
"tranquility of the whole Realm.

"Given under our Signet at My Lord's Manor of Hampton
"Court, the 12th day of October, 1537,

"JANE, QUEEN."

It will be noticed that neither in this letter nor in the doctors' certificate is mention made of any operation.[10] Nor is any previous incision of the abdomen referred to in the description of the emblaming,[11] a process rendering necessary an abdominal section with complete evisceration of abdominal contents. Negative evidence as this is, it does not, however, prove that Cæsarian section was not performed. One frequently hears of major operations being performed with complete success in country places, without the semblance of antiseptic precautions, the atmosphere itself being perfectly aseptic. This may have been the case at Hampton Court where Queen Jane was confined. The Plague was raging in London, but the King issued stringent injunction that no one from the infected City was to approach Hampton Court during the Queen's confinement.[12] That the Queen did well for at least a week after her delivery is shown by the fact that the King proposed to leave her, but altered his plan when the case took an unfavourable turn a few days before death. What was the cause of this unfavourable turn eight or ten days after a successful delivery? Assuming that Cæsarian section had been performed, may it not have been that the wrappings with which the patient had been swathed, were removed for the first time and then, through want of cleanliness, septic peritonitis induced? The existence of peritoneal effusion is perhaps indicated by the expression in the doctors' report that after a "natural lax" the patient "began to lighten."

While, therefore, it might be rash to assume Cæsarian section had taken place it might be equally rash to assert the contrary. Rumours concerning exalted personages do not take a firm hold in the public mind without, as a rule, some ground. That the belief in Queen Jane's delivery by the Cæsarian section was strongly held

is shown by the ballads written at the time, some of which are here reproduced.

(1) From Miss Strickland's "Life of Queen Jane."

"When as King Henry ruled this land,
He had a Queen, I understand,
Lord Seymour's daughter, fair and bright;
Yet death, by his remorseless power,
Did blast the bloom of this fair flower.
O mourn, mourn, mourn, fair ladies,
Your Queen, the flower of England's dead.

"The Queen in travail pained sore,
Full thirty woeful hours and more,
And no ways could relieved be,
As all her ladies wished to see.
Wherefore the King made greater moan
Than ever yet his Grace had done.

"Then being something eased in mind,
His eyes a troubled sleep did find,
When dreaming he had lost a rose,
But which he could not well suppose
A ship he had a "Rose" by name,
Oh, no, it was his Royal Jane.

"Being thus perplexed with grief and care
A lady to him did repair,
And said, 'O King, show in thy will
The Queen's sweet life to save or spill.'
'Then as she cannot saved be,
Oh, save the flower though not the tree.'
O, mourn, mourn, mourn, fair ladies,
Your flower, the Queen of England's dead."

(2) From "Notes and Queries," 2nd Series, xi, 131.

"Oh women, oh women,
If women ye be,
You'll send for King Henry
To come and see me.

"Oh, King Henry, King Henry,
If King Henry ye be,
You'll send for the doctor
To come and see me,

"Oh Doctor, oh Doctor,
If Doctor ye be,
You'll open my right side
And save my baby.

"They churched her, they churched her,
They dug her her grave,
They buried her body,
And christened her babe."

N.B.—It will be noticed that in the above rhyme a right-sided laparotomy is indicated.

(3) From "English and Scottish Ballads," by Francis James Child.

(Extract): "The surgeon was sent for; he came with all speed,
In a gown of black velvet from heel to the head;
He gave her rich caudle, but the death sleep slept she,
Then her right side he opened and the babe was set free.

"The babe it was christened and put out and nursed,
While the Royal Queen Jane lay cold in the dust."

(4) A Scottish Version (from the same.).

"Queen Jeanie, Queen Jeanie, travelled six weeks and more
Till women and midwives had quite given her o'er.
'O, if ye were women as women should be,
Ye would send for a doctor, a doctor to me.'

"The doctor was called for and set by her bedside,
'What ails thee, my ladie, thine eyes seem so red?'
'O doctor, O doctor, will ye do this for me,
To rip up my two sides and save my babie?'

* * *

"But with sighing and sobbing she's fallen in a swoon,
Her side it was ripped up and her babie was found.
At this bonnie babe's christening there was mickle joy and mirth,
But bonnie Queen Jeannie lies cold in the earth."

N.B.—It will be noticed that in all these rhymes the Queen showed a strong desire to save her child's life.*

* It need scarcely be said that Hampton Court Palace is haunted by the ghost of Queen Jane. On each anniversary of the Queen's death, at midnight, the apparition, in orthodox style, clad in a shroud, and holding a taper, passes along a corridor and enters the room in which the confinement took place.

PHŒNIX CREST
Granted by HENRY VIII
to the Seymour Family
to commemorate the
death of Queen Jane Seymour
in giving birth
to King Edward VI.

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1. Ramsbotham, Francis. "Principles and Practice of Obstetric Medicine and Surgery."
2. Pliny. "Natural History," Book viii., Chap. 9.
3. De Cauliac. "Chirurgia," Paris, 1363.
4. Rusett, Francois. "Traite Nouveau de l'Hysterotomotokia," Paris, 1581.
5. The fullest history of this operation is perhaps that contained in Cooper's "Surgical Dictionary," 1838.
6. "Macbeth," Act V., Scene 7.
7. "Dictionary of National Biography."
8. Strickland, Agnes. "Lives of the Queen's of England."
9. Fuller's "Church History." The original is one of the Cottonian MS.
10. This letter will he found in the Cottonian MS. The date of the Queen's letter to the Privy Council is erroneously given by Fuller as October 22 (two days before the Queen died). This mistake has been repeated by Ramsbotham.
11. State Papers. Domestic Series, No. 1060.
12. State Papers. Domestic Series, No. 893,

Reminiscences of Lawson Tait.[1]

By CHRISTOPHER MARTIN, M.B. (Edin.), F.R.C.S. (Eng.),

Senior Surgeon, Birmingham and Midland Hospital for Women, President of the Society.

WHEN you did me the honour of nominating me for the post of President of your Society, I felt that instead of addressing you on some obstetrical or gynæcological topic, it might be more interesting if I gave you some of my personal reminiscences of the greatest of all Birmingham gynæcologists, Lawson Tait.

I was intimately associated with him from 1889 to 1893—the very acme of his career—as pupil, assistant and partner.

In July 1889 I came down from Edinburgh with a letter of introduction from Prof. Sir Alex. Simpson (whose house surgeon I had been), and became one of Mr. Tait's pupils. It was his custom to take a limited number (usually four) of post graduate pupils, who each paid him a fee of from fifty to one hundred guineas for a period of three to six months. These pupils were mostly Americans, and he told me "he had to charge a fee to keep out the crowd." They were not all Americans, for I can recall, amongst others, Morse of Norwich, Septimus Sunderland of London, Tenison Collins of Cardiff, Hawkins Ambler of Liverpool, John Campbell of Belfast, Albert Morison of Hartlepool, and Stewart Mackey of Sydney. I believe also Thomas Wilson was a pupil for a time. Within a week of my arrival in Birmingham I fell ill with scarlet fever, and was in hospital for six weeks. When I was convalescent Mr. Tait kindly took me down to his beautiful house, in the New Forest, to recuperate. He used to come down most week ends, and so we got better acquainted. About this time he quarrelled with his private assistant, Mr. Teichelmann, and offered me his post, which I gladly accepted. In May 1890 a vacancy occurred on the staff of the Women's Hospital, and I was appointed almost entirely through his influence. In 1891 he took me into partnership; and the same year my brother Charles joined us as our joint assistant. So much for the way I became connected with him.

1. A Paper read before the Midland Obstetrical and Gynæcological Society on October 14th, 1920.

He has been dead over 21 years, and therefore most of those present never saw him. But once seen he was not easily forgotten. He was a short, stout man with a magnificent head, thick bull neck, corpulent body, podgy legs, and small hands and feet. Someone—I forget who—described him as "a man with the body of Bacchus and head of Jove." He had a small, beautifully shaped mouth, a firm chin, and eyes which had a wonderful power of fascination. His voice was soft and musical—I have heard him sing sweetly—but when enraged he could roar like a lion. He had a very big head—he took "8" in hats—and a fine head of hair just beginning to turn grey.

He was a man of great force of character, great will power, great genius. By his personal magnetism he dominated all with whom he came in contact, certainly all those in his service. They worshipped him and would do anything for him. In this respect, as in many others, he resembled Napoleon. He was a man of untiring industry and immense vitality and energy. He never spent an idle moment. He had many interests—inside and outside his profession—many irons in the fire at once; and the amount of work he got through was marvellous.

Let me describe a typical day's work. He was called at 7 a.m., had a very light breakfast in bed of tea and bread and butter, had his bath, and was usually down about 8 a.m. He ran rapidly through his morning letters (and they were numerous) and dictated replies to his secretary. At 8.30 a.m., with a big cigar in his mouth and a sheaf of papers in his arms, he got into his carriage—the familiar Victoria with two grey horses—picked up his assistant, and drove off to the Women's Hospital at Sparkhill. Here he would do from one to three operations, and be back at his house in the Crescent about 11 a.m. There would be here probably one or two more operations; and then about noon he would get his lunch. This was always a substantial, but not heavy, meal. From 12.30 to 3 or 4 p.m. he had consultations at home; and I need not tell you how thronged his rooms were. He was a man of few words, grasped very quickly the gist of the patient's story, and was equally quick in his examination and diagnosis. His abdominal examination would take less than a minute, his vaginal examination was just as rapid; and then he had made up his mind as to his diagnosis —right or wrong. He wasted few words on his patients. He told them briefly and abruptly what was wrong and what must be done; and they "could take it or leave it." He was no respecter of persons, and never toadied to the rich or great. I have known him miss a very big fee by losing his temper with a foolish, talkative woman. On the other hand, he was most generous to the poor. He took scores of poor women into his Private Hospital,

keeping them there for four to six weeks, and operating on them for nothing. He made no difference in treatment or food between them and those who were paying him handsome fees.

His consultations over, he would rush out perhaps to see out-patients at the Women's Hospital, perhaps to a Committee meeting at Mason College, the Medical Institute, or elsewhere. Then may be, he would drive out to a consultation in the country and be back for dinner at 7 p.m. After dinner, he might read a paper at a medical society, or take part in a debate. On returning home he would perhaps sit down and sketch out a medical article or indite to his secretary a scathing letter to be sent to the *British Medical Journal* in reply to some antagonist. He revelled in such wordy warfare and "drank delight of battle with his peers." My brother Charles was his private secretary for over a year, and was often successful in toning down some of his most fiery letters. Mr. Tait would rush into the library, fling down a letter and say: "Write to this man and tell him I'll see him damned before I'll do what he wants." The letter when typed would perhaps read: "Mr. Lawson Tait deeply regrets that he is unable to accede to Mr. B's request." "But that is not what I said, Charlie," Mr. Tait would exclaim when he came to read the letter. "No, but it means the same thing and reads better," my brother would reply; and the amended letter would be sent.

He was very clean in his person, dressed for comfort rather than appearance, and did not care a straw what people thought or said about him. In the house and in his consulting room he usually wore a black velvet lounge coat. He never played cards, chess, billiards, or golf. He enjoyed the good things of this life, but he was neither a gormandiser nor a drunkard. He was, however, a heavy smoker and consumed innumerable strong cigars. He was fond of the theatre, and numbered many leading actors, such as Irving and Toole, among his intimate friends.

He had many hobbies and derived keen pleasure in pursuing them. His house was full of curios, especially Chinese and Japanese. I remember one evening when the Honourable Hugh Fraser (the British Minister to Japan) dined with him, and I was asked to join the small party. The conversation turned to Japanese curios and especially ladies' combs. Mr. Tait left the room and brought down several drawers full of these articles—there were scores of them—which he had picked up, arranged, put away, and almost forgotten.

He had in his house many beautiful Catholic emblems, crucifixes, triptychs, and pictures. He once told me that he was brought up as a Catholic and, as a boy, sang in the choir

and acted as the priest's attendant or server at the office of the Mass. Though in after life he ceased to attend the services because he no longer accepted its doctrines, up to the day of his death he had a great affection for the Roman Church and a love for all forms of Catholic art. He once delivered a sermon in the Church of the Saviour "On the Image of Baal," in which his religious views were boldly expressed. From it we gather that they were those of a Unitarian, but certainly not an Atheist.

He was passionately fond of animals and always had a large number of cats—especially blue Persians. His love of animals led him to take up an extreme position with regard to vivisection, which he denounced in no measured terms. He abominated every form of sport that involved cruelty to animals, such as fox hunting, pigeon shooting and grouse shooting. But he did not object to fishing; and, at one time, had a fishing cottage at King's Bromley, where he used to go for the week-end. It is still in existence, a black and white half-timbered bungalow, now run, I believe, as a tea house.

He was fond of the country and, whenever he could, got out of Birmingham. He had, in addition to the fishing cottage and his house in the New Forest, a bungalow out at Yardley Wood, a half timbered house at Cropthorn called "The Den," a sailing yacht on the Solent, a steam launch and a house-boat on the Avon. Here his happiest hours were spent, and he was never merrier than when entertaining a few bosom friends, and especially in cooking for them. I remember well he once took a party of friends, including the late Dr. Saundby, up the river from Worcester. Dr. Saundby and I were at the prow; and, as the launch went up stream, we noticed we were getting into very shallow water. We shouted back to warn Mr. Tait, but he was busy cooking in a frying pan our lunch, a weird mixture of eggs, cheese, tomatoes, onions, and potatoes. Suddenly the stern grounded, the current swept the boat sideways, and we were nearly capsized. As it was, the frying pan and its contents were upset and spoilt. Mr. Tait called us a pack of damned fools, seized the tiller and got us safely to the shore. We then scrambled out and sat on the bank whilst he proceeded to cook another lunch for us in the boat.

Speaking of Saundby reminds me of a characteristic incident. Tait read a paper at the Midland Medical Society, I believe on Appendicitis, and, as was his wont, invited several doctors (including Saundby) to dine with him before the meeting. Well, after the paper there was a rather heated discussion; and Saundby and Tait flatly contradicted each other's statements. Finally, Saundby blurted out, "Really, Mr. Lawson Tait is the rudest man I know." Tait at once retorted, "It is very strange that Dr. Saundby cannot

open his mouth without insulting somebody." Truly a case of the pot and the kettle!

He was an able and convincing speaker and debater, ready in retort, quick to see the weak points in an opponent's arguments, and clever in concealing his own. Some of you may remember a debate on the "Germ Theory of Disease" at the Medical Institute in 1895. He had the whole of the local surgical talent against him—Jordan Lloyd, Priestley Smith, Morrison, Barling, Leedham Green, etc.—all tearing his arguments to pieces. But he was a match for the lot of them and came out of the debate triumphant; though we all knew he was wrong and they were right.

Another occasion on which he gained an intellectual victory over his opponents was in the action for libel Dr. Denholm brought against him at the Manchester Assizes. He had some of the ablest of the Manchester medical men arrayed against him—Whitehead, Lloyd Roberts, Dreschfeld, Reynolds, Japp Sinclair and others. The case looked very black; but when he got into the witness box he refuted their arguments and statements so convincingly that both Judge and jury were won over to his side and the case against him collapsed ignominiously.

He was a hater of hypocrites, humbugs and cowards; but in his heart admired those who had the courage to stand up to him. I remember once he went into a patient's room and rang the bell several times for a nurse, but no one came. He stormed out of the room and down the corridor to the nurses' sitting-room. There he met a new nurse—an Irish girl—who had just joined his staff. "Where the devil have all the nurses got to?" he roared. "I'm damned if I know, sir," she calmly answered. This "soft" answer turned away his wrath and rather pleased him than otherwise.

He was an ugly enemy; and when he hit he hit hard, and did not mind whether it was above or below the belt. He was fond of rushing into print, both in the local press and the medical journals. Some of his controversies with Keith and Spencer Wells in the *British Medical Journal* between 1889 and 1892 were acrimoniously conducted on both sides, and the letters were very pungent and scathing.

In private life he was a charming companion, and it was a pleasure to listen to his conversation. Some of the most interesting hours I have spent were at his dinner table, where he entertained all sorts of guests—Kropotkin the Nihilist, Prof. Blackie of Edinburgh, Alfred Hayes the poet, Toole the actor, Hugh Fraser the diplomatist, Canon O'Sullivan of Solihull, and others. It was indeed a treat to listen to them, with their wit and repartee and their merry stories. I only wish I had recorded some of the latter.

He had a violent temper and when he let himself go was like a

raging bull. I remember once he got into a passion with a telephone operator; and, as he could not lay hands on him or her, he tore down the instrument from the wall and smashed it on the floor. Needless to say his blind rage cost him dearly both in inconvenience and loss of time.

He was not often ill, but when he was he was difficult to treat and manage. On one occasion, Mr. Gilbert Barling (as he was then) had to remove a calculus from his urinary tract. Dr. Harmer gave the anæsthetic; and Mr. Tait took it very badly, went black in the face, and nearly died. Well, immediately after the operation, Mr. Barling went off for his holiday and left him in my charge. Needless to say, I told him to keep to a bland milky diet and to stay absolutely in bed. Would you believe it that, when his friend Dr. Donovan called next day, he found him sitting in an armchair by the fire in his dressing-gown with a Tam o'Shanter on his head, a pint of champagne at his elbow, and a big cigar in his mouth. "Hullo!" said Donovan, "is this allowed?" "Oh yes," said Tait, "Christopher ordered it!" In spite of this and of his refusal to allow me to use antiseptics to the wounds, he managed to recover. On the fifth day he got up and insisted on leaving Birmingham and driving out to his bungalow at Yardley Wood—against Mrs. Tait's entreaties and my protests. After his arrival he sent me a defiant telegram: "Arrived safely, temperature normal, had beef and pickles for dinner."

He was a man of great physical strength and tremendous energy, both bodily and mental. I think he was able to do so much work because of his marvellous faculty of sleeping. He could sleep anywhere and at any time. He had often to take long railway journeys. One day he might be called down to operate in Southampton; and, next day, as soon as he got back, be summoned to Inverness. He slept nearly all the time in the train and would arrive after a long night's journey as fresh as a daisy. I have often seen him finish an operation and sit down and fall sound asleep whilst the second case was being anæsthetised.

As an operator he was wonderful. He worked without the least appearance of haste and with marvellous rapidity and dexterity. He was seen at his best in a bad case of pyosalpinx or a hysterectomy for myoma. Though he encountered appalling difficulties he proceeded silently, swiftly and undauntedly to a triumphant issue. He used no antiseptics but trusted to simple soap and water cleanliness. This was, I think, the great mistake of his surgical career. Had he only accepted Lister's teaching and done his operations under more aseptic conditions his results (good as they were) would

have been marvellous. But he was obstinate, and up to the last refused to accept and practice what he called "Listerism."

What he did for gynæcology and abdominal surgery is known to all. Amongst other achievements I would recall that—

(2) He reduced the mortality of ovariotomy by discarding the "clamp," simply ligaturing the pedicle and dropping it.

(2) He was the first to remove gall-stones by operation.

(3) He was the first to operate for tubal pregnancy.

(4) He was the first to remove the uterine appendages for inflammatory disease.

(5) He devised a new, simple and speedy method of repairing the perineum.

(6) He introduced washing out and draining the perineum for peritonitis.

(7) He was the first to suggest Cæsarean section for placenta prævia.

Lawson Tait was undoubtedly the greatest surgical genius who ever practised in Birmingham. That he had many faults I will not deny. But who is perfect? "Let him that is without fault cast the first stone." Let us bury his failings with him in his grave; but let us cherish the memory of the good he did, of his pioneer work in gynæcology and abdominal surgery, of the incalculable services he rendered to mankind. "We shall not look upon his like again."

CLINICAL REPORTS.

Acute Hepatic Toxæmias Complicating Pregnancy and Labour.

By Sir JOHN PHILLIPS, M.A., M.D. (Cantab), F.R.C.P. (Lond.),

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OF late years much attention has been paid to the bacterial infections of the liver, but no marked stress has been laid upon the liability of the liver and possibly of the pancreas to become specially infected during the pregnant condition. Moreover, no discussion on this subject appears to have taken place at any meeting of the Obstetrical Society. The chief infections appear to be from the colon bacillus and less frequently possibly the staphylococcus and the streptococcus. There is no doubt, in my own experience, that the first is the most frequent; and the five cases which I have detailed below represent all my experience of this complication. In one case (i) a question of opinion as to whether the disease was acute yellow atrophy or an acute ascending toxæmia has arisen. The symptoms are so much alike that I have ventured somewhat fully to report this case, with post mortem, to show the difficulty of making a certain diagnosis.

CASE I.

The patient, a primigravida, aged 32, had been married 9 years, but with no previous pregnancy. She had diphtheria four years previously, but it was followed by no bad sequelæ. She was always a delicate girl, and wore leg-irons when young. When first seen with Dr. Des Voeux her height was 5 ft. 2½ ins.; she was a small, thin, but well-formed brunette. External pelvic measurements were found to be: interspinous 8¼ inches, intercristal 9½, external conjugate 6¾. During the whole of the pregnancy she suffered from much sickness, and with hot burning pain (like severe indigestion) behind the sternum, especially at night. The urine contained neither albumen or sugar. She was watched regularly

after the 30th week, and at the 32nd week a breech presentation changed suddenly to a vertex (la culbute), the patient herself being conscious of it. At the 34th week the vertex barely entered the brim; chloroform was therefore given as the patient was intolerant of pain. The cervix was found to be long and rigid: it was dilated sufficiently to introduce the finger, and a bougie was then inserted between the membranes and the uterine wall. Labour pains came on 48 hours after the insertion of the bougie and labour speedily terminated without any difficulty, the child being stillborn for no apparent reason.

The progress of the patient after labour was very unsatisfactory, constant sickness being the most marked symptom. At the end of 18 hours she began to vomit brownish blood: faint jaundice then set in for a few hours and nearly disappeared later, and she died 48 hours after labour, the temperature rising to 110°F. shortly before death, having been down as low as 93°F. twelve hours previously, the pulse becoming increasingly rapid (90 to 164 per minute); her tongue was dry and cracked, sordes on the lips, her aspect was drowsy and she was very restless and continuously moaning.

Treatment consisted in administering copious subcutaneous injections of saline with dextrose, but they seemed to have no effect whatever on the progress of the disease.

Post mortem by Dr. Trevor 16½ hours after death. Blue staining of the face and abdominal wall present. The stomach showed considerable gastritis, as evidenced by adherent tenacious mucus and some pigmentation. There were small submucous hæmorrhage and about half a pint of fluid blood mixed with the contents of the stomach. There were lines of blood pigment over the longitudinal veins at the lower end of the œsophagus. The spleen was small. The liver weighed 36 oz. Most of the right lobe showed chronic venous engorgement, but there were some distinct areas of apparent acute yellow atrophy.

Microscopical Examination.

The capsule of the liver shows a fine wrinkling and is thrown up into small folds.

Under the low power the lobular arrangement can in many places still be made out owing to the preservation at the periphery of the lobule of a very narrow zone of liver cells, which stain fairly well. In these areas the central vein of the lobule is distended and the liver cells immediately surrounding it have necrosed and practically disappeared—a definite nutmeg change. In the intermediate zone liver cells in all stages of degeneration are seen.

Under the high power, some show hydropic degeneration, others cloudy swelling, and others again are merely masses of vacuolated

protoplasm with no visible nuclei. Many of the cells are loaded with granules of bile pigment.

The normal arrangement of the columns of the liver cells is destroyed and the cells lie separate and distinct. The capillary network is distorted and not easily made out. Scattered throughout the section are large cells loaded with dark granules of large size. Some of these appear to be in the capillaries and are phagocytic cells with inclusions of cellular and nuclear debris.

In these areas, the picture is that of an advanced nutmeg liver together with superadded degeneration of the liver substance.

In the yellow parts of the liver the microscopical changes are similar, but here the topography of the section is blurred and the liver lobules can no longer be made out. Here and there in the portal spaces the connective tissue is cellular, but no diffuse increase in the interstitial tissue of the liver has occurred, neither are there any newly-formed bile canaliculi. There are, however, in those places where the liver cells are fairly well preserved, isolated cells here and there containing two nuclei. No crystals of leucin or tyrosin are seen in the section.

On the whole the appearances are not typical of acute yellow atrophy, but they might be interpreted as being those of a very early or commencing stage. I would prefer to regard them myself as degenerative and associated with some general grave toxæmia, for, as the material for examination was not obtained until some seventeen or eighteen hours after death and the patient died with a temperature of at least 110°F., I am of opinion that much of the change present is of post mortem occurrence and of autolytic nature. The disturbance of the relationship between the liver cells makes a certain statement as to the condition of the intercellular bile ducts impossible, in spite of careful examination with an oil immersion objective, but it is more than likely, seeing the loaded state of many of the cells with bile, that they were obstructed. The larger ducts in the portal spaces certainly show catarrhal change. The jaundice would then be of hæmohepatogenous type, such as is met with in many grave septic or toxic states.

CASE II.

A primigravida, aged 32, was confined of a stillborn child, weighing 9 lbs., forceps being applied at the brim; light chloroform anæsthesia carried out for about six hours—on and off—and full anæsthesia for about two hours; no difficulty with the placenta. For 24 hours the temperature remained normal and the pulse quiet. The urine had been examined and found normal just before labour. On the second day there was slight general jaundice, the urine being markedly stained with bile, and she passed dark-coloured

fæces, probably old blood. She then became slightly drowsy and failed to recognise friends around her. The urine was later found to contain much bile and a trace of albumen; it was also hyperacid.

When I saw her in consultation, the pelvic conditions were quite normal; lochia abundant and of good colour and involution rapid. The patient was a high-coloured brunette, with a slight general tinge of jaundice, very drowsy, not answering questions; she scratched her face from time to time with her left hand and only swallowed food if placed in her mouth; the pulse was quick, 130, gradually becoming smaller; temperature varying from 99°F. to 100°F. The liver was certainly tender, as she flinched when the hepatic region was manipulated. No definite enlargement could be made out. Saline injections had been given continuously without any good effect. She died 48 hours after labour, in a comatose condition.

Case III.

A primigravida, aged 23, with general pelvic contraction, was seen on June 29, 1914, when 35 weeks pregnant. The breech was found presenting. The patient was accordingly put into a modified Trendelenberg's position and an external version carried out. It was then found that the vertex would barely enter the brim: accordingly the cervix was dilated and two solid No. 10 elastic bougies inserted between the membranes and the uterine wall: she was not feeling well at the time and had noticed that her motions were very grey in colour; her temperature was 100°F. and her pulse 94. Within 24 hours her temperature went up to 102°F., and it was thought advisable to remove the bougies. Labour came on slowly and an occipito-posterior position was found: rotation with forceps and delivery resulted in the birth of a healthy female child, weighing 6 lbs. A double episiotomy was necessary to save the perineum. During the next 24 hours she was very restless and sick, and became slightly jaundiced. A dose of castor oil produced a large white clay-like motion. The sickness and restlessness continued and the jaundice increased during the next 24 hours, lochia and involution meanwhile going on quite normally. Her temperature varied between normal and 100°F. at night, and her pulse varied between 96 and 112: she looked and felt very ill, and on the 6th day a slight deepening of the jaundice occurred. Swabs taken from cervix on 2nd and 6th day were found to be sterile. Her urine contained a large amount of bacterium coli. Sir Bertrand Dawson, who saw her with me, advised small doses of grey powder and rectal injections of saline solution, but it was not until the 6th day that a little bile was noticed in the motions, and it

was not until the 12th day that they became bile-stained. On the 18th day they were normal.

Involution was quite rapid, and the lochia ceased at the ordinary time. Her temperature became quite normal about the 16th day, her appetite returned and the jaundice gradually disappeared.

The child vomited much yellow mucus during the first 24 hours and was jaundiced, this being increased during the next 24 hours; all the vomit was deeply stained yellow, as was also the urine; drowsiness was a marked symptom. No bile came through the bowel until the 10th day, and the jaundice disappeared on the 21st day.

The patient was confined a second time without any of the complications above mentioned, but the child was even more deeply jaundiced when born than the former one, and for seven days the urine was brightly stained with bile and nothing but meconium and colourless mucus passed by the rectum. It was considered that the child had either bacteriological catarrh or possibly congenital absence of the hepatic ducts. Fortunately the bile appeared the 12th day in the motions, and about that time the jaundice gradually faded and the patient convalesced.

CASE IV.

The patient, aged 20, a primigravida, was under the care of Dr. Lumsden; she was healthy, but most of her life had suffered from bad sick headaches if she got excited or tired. Her husband had developed, a few days before her illness began, what was thought to be an influenza chill; jaundice developed and was still present at the time of the labour, but he made a good and easy recovery. The patient a few days later got an apparently similar chill, and three to four weeks before term arrived in London, feeling, as she said, "desperately ill." The patient had slight yellowish discolouration of the skin and had noticed greyish-white motions for two days. Her sister developed general jaundice three weeks later at the same country residence. The labour was quite normal and easy, being about three or four weeks before full term; very little chloroform was necessary. The child, although premature, was alive and vigorous; the motions passed during the labour were white and constipated, and it was noticed that her slightly jaundiced skin was everywhere very sensitive. During the first 24 hours post partum the patient was very sick and declined food, while the icteric tint, which was general, slightly deepened. At the end of 48 hours she became drowsy and began to scream more or less continuously, with a few minutes interval; the head was retracted and she was perpetually rubbing the occiput on the pillow, like a child with tubercular meningitis. The lochia and involution were

normal in every way; the urine was passed unconsciously, and a catheter specimen showed bile staining and very marked bacterium coli infection, but no leucin or tyrosine. She was quite unconscious, with marked patella reflex and a big-toe clonus. On the 4th day the jaundice was deeper, she was more restless, the pulse quicker, and she resisted violently any attempt at rectal nutriment. The temperature varied between normal in the morning and 101°F. at night. On the 6th day the jaundice was less, the screaming had almost ceased, and the head and limbs underwent peculiar rhythmic movements, so that the skin became quite red and sore. On the 7th day the screaming had quite ceased, the jaundice of the skin was less, but the urine was still deeply stained and the motions were white. She now became semi-conscious, but the rhythmic movements were still present. The next day she was quite conscious and taking food naturally. On the 9th day, at the site of the puncture in the right thigh, made for saline injections, a large abscess formed without any corresponding rise of temperature; the pus being let out gave a pure culture of bacterium coli. For about three weeks, and until her complete recovery, an autogenous vaccine of the B. coli was administered regularly to the patient.

Sir Bertrand Dawson saw the patient on several occasions, and considered the case one of ascending infection of the bile ducts.

Her mental condition was peculiar: she remembered arriving at the house just before the labour and seeing her own doctor, but forgot everything afterwards for 8 days, nor has her recollection of what occurred during that interval returned. The perineal sutures had not united, and later a posterior colporrhaphy was performed with a good result.

The treatment consisted in continuous subcutaneous injections of saline, dextrose, and when possible rectal salines. Paraldehyde was the only drug which appeared to give her any rest or sleep: it was given in large doses. The temperature was never high, being 101°F. on the 4th day, and it became quite normal on the 10th; the pulse varied between 100 and 130 during the whole of the illness.

The child was not born jaundiced, nor did it develop this condition later.

Case v.

A very strong and healthy primigravida, aged 34, was under the immediate care of Dr. Beauchamp. Twenty-four hours before labour started she felt very unwell and was sick; she had noticed the motions were very pale ("like clay"). She was sick during the whole of the labour, bringing up at first a frothy mucus of a bright

yellow colour. At the end of 24 hours, and during the second stage, she vomited up a large amount of dark brown material, which contained no food and was proved to be altered blood. The presentation was a vertex (occipito-posterior) in the 3rd position; rotation with the forceps and delivery was carried out. During the operation she vomited up nearly half a pint of the same black material. She complained of severe pain behind the sternum; 24 hours after labour she was very apathetic, with a pulse of 94, but a normal temperature. The liver was enlarged and the hepatic area tender to the touch. Jaundice of the conjunctivæ and skin now developed and emphysematous crackling appeared over the right neck and chest, with marked puffiness of the subaxillary region on the same side. She was unable to take any food, was very restless and apathetic and was sick when any attempt at feeding was made; the action of the bowels were still clay-coloured. The restlessness continued for another three days and she still complained of feeling very ill: the urine, which had been very dark-brown in colour, cleared up at the end of the 20th day; bacteriological examination showed the presence of a large amount of bacterium coli. Swabs taken from the cervix on the 3rd day were found to be sterile. The jaundice disappeared and the motions became normal at the end of the third week. The lochia and involution were normal throughout.

The child was not jaundiced, but developed a slight attack 24 hours post partum.

I have related the above five cases somewhat in detail as they appear to present very distinctive features. Every practitioner is cognisant of the slightly muddy complexion, scarcely amounting to jaundice, with malaise, which frequently attack the lying-in woman within 48 hours of labour, and I have come to believe that many of these are in all probability minor infections as compared wtih those related above but of the same type.

Jaundice must be looked upon merely as a symptom, and it occurs more or less deeply in acute yellow atrophy, hepatic toxæmia, Weil's infective disease, late chloroform poisoning, and as the result of certain metallic poisoning, *e.g.* phosphorus. In a similar manner the slight jaundice occurring in the above detailed cases should be considered as one symptom in a train of a series of graver ones.

The yellow staining occurring in these cases is much less than in simple icterus, and I have thought that these cases should be classed under hepatic toxæmia rather than the jaundice of pregnancy, as more indicative of their true pathology.

It will be noticed that only in one case (No i) was a post mortem

obtained, and even in this a definite conclusion was not arrived at, for it will be noted that Dr. Trevor thought that the appearances were not typical of acute yellow atrophy, but they might be interpreted as those of a very early or commencing stage, while Sir Humphry Rolleston, who saw her with me, in a letter to me on the matter afterwards, says: "In the light of the clinical symptoms, post mortem, and microscopical sections, I regarded the case as one of acute yellow atrophy, fatal at a very early date, probably because the patient had very little resistance."

Case No. ii was probably one of profound toxæmia, due to some hepatic or possibly pancreatic infection, and her condition appeared to be hopeless from the first.

In Case No. iv several interesting points are to be noted. First of all, the three cases of slight jaundice occurring in one family in the same house within a short time of each other; secondly, the loss of memory of events from shortly before the labour until eight days had elapsed; thirdly, the cerebral symptoms coming on within 48 hours of the labour; and, lastly, the proof by bacteriological examination that the poison was due to bacterium coli. A diagnosis was made of an acute ascending infection of the bile ducts, with cerebral irritation, due to the presence of bacterium coli. This case tends to confirm the theory of Bardinet, who, in 1863, declared that jaundice may be produced as an epidemic among pregnant women, and describes such an epidemic: of 13 cases notified, three ended fatally and seven children survived. Kirksig (*Hufeland's Journal*, Bd. vii, hf t. 3, s. 94) also mentions an epidemic of 70 cases, five of whom were pregnant, two aborted and three died.

Case No. iii was also typical of a similar infection. Here again we have the white motions, irritability and tendency to coma, combined with slight jaundice, while examination of the urine showed the presence in large quantities of the bacterium coli. The symptoms so closely imitated those of late chloroform poisoning that during the earlier days of the illness a diagnosis of that state was made.

In Case v many symptoms of acute yellow atrophy were present, such as the dark-brown vomit of altered blood, the tenderness over the liver, slight jaundice, with the sickness, restlessness and apathy so characteristic of acute yellow atrophy. Here, too, the urine was found to be loaded with bacterium coli.

All the five cases occurred in primigravidæ and at or about the time of onset of labour; albuminuria, as is well recognised, also usually occurs in women pregnant for the first time.

I have notes of two additional labours occurring in the same patient ten and twelve years ago and before the bacteriology of the puerperium was at all worked out. I am therefore unable to say

anything as to the presence or not of the bacillus coli and have not included them in this series, but the patient at both her labours presented all the symptoms of the above five cases, of which I made accurate notes at the time and of the various opinions which were given by the physicians who saw her. As some slight confirmation of my surmise I may mention that five years ago, while treating this patient for a slight local ailment, I had an opportunity of obtaining a catheter specimen of her urine and it was loaded with B. coli.

The sum total of the five cases shows a fatal result in two cases within 48 hours, and recoveries in the remaining three after several days' illness.

With regard to the children, on two occasions (Case iii) the child was either born jaundiced or developed it rapidly after delivery, and aroused the suspicion that possibly the bile ducts might be in some way congenitally stenosed. Two were stillborn without any apparent reason.

The liver, as Rolleston points out, is peculiarly susceptible to morbid changes during pregnancy, and there is reason to believe that necrotic changes in the peripheral zone of the lobules of the liver play a very important part in the production of puerperal eclampsia.

Whitridge Williams (*Johns Hopkins Hospital Bull.*, 1916, xvii, p. 71), in reporting 12 cases of pernicious vomiting of pregnancy and having acute yellow atrophy, insists on a distinction between eclampsia in which necrosis occurs in the peripheral zone and acute yellow atrophy in which this process begins in the intermediate zone of the lobule.

The difficulty of making a differential diagnosis between acute yellow atrophy, malignant jaundice and the group I have reported will be seen on perusing the five detailed cases. Some confusion appears to exist as to whether acute yellow atrophy and what is termed malignant jaundice are similar or separate diseases. Bristowe (*Theory and Practice of Medicine*, pp. 794 *et seq.*) describes the leading characteristics of the two former (which he considers one and the same disease) as vomiting, especially of a coffee-ground fluid, due to gastric hæmorrhage, intense headache, irritability and restlessness.

The question therefore arises whether the cases I have brought forward should be included among instances of mild acute yellow atrophy—I am inclined to oppose this idea.

As long ago as 1863 the connection between pregnancy and acute yellow atrophy was recognised, and at a meeting of the Berlin Obstetrical Society in that year an interesting discussion took place. Virchow stated that he had never seen a case of jaundice in

pregnancy ending fatally. (*Monatsschrift für Geburts.*, 1863, Hft. 2, s. 89.)

M. G. Wells (*Archiv. of International Med.*, Chicago, 1908, p. 594) points out that one of the forms of delayed chloroform toxæmia resembles acute yellow atrophy.

In considering this subject, Dr. Harold Low has kindly allowed me to quote from an unpublished paper of his, entitled "So-called Delayed Chloroform Poisoning." The symptoms mentioned show how difficult a diagnosis may become.

The exact origin of the condition is still a matter of uncertainty; certain facts, however, are recognised: (1) Prolonged chloroform narcosis produces in animals changes in the liver, similar to those of acute yellow atrophy; (2) acidosis or acid intoxication is present, especially in children, in conjunction with narcosis; (3) in patients dying subsequent to anæsthetisation by chloroform, the liver sometimes shows well-marked degeneration similar to that observed in acute yellow atrophy or phosphorus poisoning. Clinically, in adults, jaundice may be marked, but it may not infrequently be absent, even in fatal cases.

There are doubtless many cases which recover, although it is extremely difficult to make a definite statement on this point.

The cardinal symptoms appear to be: (1) Vomiting coming on some hours or even days after the operation (in contradistinction to that arising immediately after or before the patient comes round from the anæsthetic). The vomit is of a peculiar coffee-ground appearance (probably due to the presence of blood). (2) The pulse steadily rises in rate and becomes progressively feebler. (3) The mental condition is one of apathy, with attacks of intense restlessness and excitable delirium (mostly, however, observed in children).

Dr. Harold Low concludes by saying: "The more I have read the less satisfactory are the theories as to what part the anæsthetic plays. The probability is that there is an unknown factor present in certain cases where chloroform has been given, producing the necrotic changes in the liver, the anæsthetic by its action upsetting a faulty metabolism."

In my cases all were subjected to anæsthesia, Case iv very slightly, the other four deeply, but I must point out that in three cases (i, iv and v) symptoms of the illness had already commenced, so that whether instances of acute yellow atrophy or acute ascending hepatic tomæmia they could not therefore have been caused by the chloroform, although this drug may probably have aggravated them.

The five cases I have detailed above are the only ones I have encountered among just over 2,000 carefully recorded cases of

labour in private practice. With regard to acute yellow atrophy, statistics are of very little value. Lomer reported 143 cases of this disease, and states that 30 of them were pregnant. Legg found 25 pregnant women among 69 cases of acute yellow atrophy, while Späth only encountered it three times in 14,061 pregnancies.

As regards the children, Lomer reported 45 stillbirths in 57 pregnancies, and in 62 cases six children were born icteroid.

The treatment adopted has been detailed in the relation of each case, and although nothing curative was suggested, yet the adoption of the remedies mentioned probably helped those patients that recovered to a more rapid convalescence.

In conclusion, I have endeavoured to show that the group of cases related (with the possible exception of Case i) has distinct features, probably due to an ascending infection of the bile ducts. It must be differentiated from acute yellow atrophy, malignant jaundice and late chloroform poisoning.

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Hysterectomy for Accidental Hæmorrhage.

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Cases of accidental hæmorrhage are classified according to their symptoms as "Concealed" or "Apparent," but a much more practical classification, so far as treatment is concerned, would be into two groups with "contractile" or "noncontractile" uteri. Fortunately the former class is much the more common and includes not only the cases with a comparatively small amount of hæmorrhage but those in which the hæmorrhage is severe but responds to treatment. If the vagina is tightly plugged or the membranes are ruptured, a tight binder applied and ergot or pituitrin given, the uterus in this class of case will contract and prevent any further serious loss of blood, but in the second class, fortunately comparatively rare, no treatment has the slightest effect on the uterine muscle which remains flabby and bleeding. Extraction of the child by the vagina or by Cæsarean section still leaves the uterus relaxed, and the only hope of saving the woman is the rapid performance of hysterectomy. Every experienced obstetrician must have had several of these cases and have recognized the utter futility of treating them on ordinary lines, the patient rapidly sinking from loss of blood and often dying while the operator still continues his manipulation.

Targett, in 1905, described a case of this nature which he had saved by Cæsarean hysterectomy, and he also mentions the two points I wish to emphasize, the presence of albuminuria and the occurrence of hæmorrhages under the serous coat of the uterus.

Amand Routh, in his exhaustive paper on "Cæsarean section in the United Kingdom," published in 1911, mentions three cases treated by Cæsarean section and hysterectomy, and considers that hysterectomy should follow Cæsarean section in those cases sufficiently severe to require this operation.

Lequeux, in 1910, advocated hysterectomy after Cæsarean section for accidental hæmorrhage in those cases "in which the

uterus is a potential danger, either as a cause of secondary hæmorrhage, or possible infection, however slight."

Phillips, in 1912, published a successful case of Cæsarean section and hysterectomy in a severe case of accidental hæmorrhage.

Shannon, in 1912, published an interesting case in which he performed this operation and found multiple small ruptures of the uterus, though he does not state whether there was free blood in the peritoneal cavity or not. He considers these ruptures to be due to over-distension.

In 1913, Essen-Möller published an important paper on this subject. He found albuminuria present in many of his cases and concluded that accidental hæmorrhage may be due either to traumatism or to a toxæmia. If the usual methods of treatment failed he advocated Cæsarean section and, if the uterus did not contract or the hæmorrhage persisted, followed this by hysterectomy.

Clifford, in 1914, published a case of accidental hæmorrhage treated by Cæsarean section and hysterectomy in which he found free blood in the peritoneal cavity. This and two of the cases I now publish, with free blood in the peritoneal cavity, are, so far as I can find in the literature, unique in this respect.

I have now performed this operation upon seven patients, in none of whom did the uterus make the slightest attempt to contract after extraction of the child (five by Cæsarean section and two per *vias naturales*), and, in six of these cases, inspection of the uterus showed such extensive extravasation of blood that complete recovery of the uterus could hardly be expected even if the hæmorrhage had been controlled.

Most of the authors I have quoted advocate hysterectomy for concealed accidental hæmorrhage, but of my seven cases only one was a case of pure concealed accidental hæmorrhage, the other six having a large amount of apparent hæmorrhage.

Case I. This patient, aged 40, was admitted to St. Mary's Hospital, Manchester, on April 22, 1914. She was nine months pregnant with her thirteenth child, and the urine was solid with albumin. She was sent to the hospital because of severe hæmorrhage for which a doctor had plugged the vagina with gauze. On admission the gauze was removed, the membranes ruptured and a tight binder applied. Labour pain soon commenced; there was no further severe hæmorrhage, and in three hours a dead male child was delivered. The placenta was delivered very soon after the child. This was followed by some large clots and then free hæmorrhage. Hot intrauterine douche, ergot and pituitary extract were given and the excessive flow of blood arrested, though a slow trickle of blood persisted. The patient was now very collapsed, and the pulse-rate had risen to 120. Three hours after delivery the Resident Obstetrical Surgeon gave another intrauterine douche, packed the uterus with gauze, injected another dose of pituitary extract, but still this trickle of blood persisted. I was sent for

seven hours after delivery and found the patient very collapsed with an uncountable flickering pulse, and a persistent trickle of blood from the vagina. I gave another hot intrauterine douche, but this had no effect upon the hæmorrhage though the uterus was apparently contracted. The cervix was not lacerated and from the whole of its internal surface, as far as it could be seen, blood was oozing, and presumably this was happening all over the uterine cavity.

I had the patient taken to the theatre and opened the abdomen in which I found about half a pint of free unclotted blood; both broad ligaments were very much swollen and almost black in colour from very large effusions of blood in the loose cellular tissue, the one on the right being the most extensive and reaching above the brim of the pelvis. The back of the uterus had several slight abrasions on it from which the free blood in the peritoneal cavity had come. I did a panhysterectomy, sutured the opening in the vagina, the round and infundibulo-pelvic ligaments and covered them with peritoneum. I had great difficulty on the right side in controlling the hæmorrhage from some small vessels ruptured high in the pelvic tissue, as the ends were lost amongst the disorganized cellular tissue, and I had to insert several ligatures round bunches of this tissue before the vessels were satisfactorily controlled. At the end of the operation I found I was perilously near the ureter, but the patient's general condition was so serious that I considered it better to run this risk than to spend any more time over the operation. After the operation we kept the patient in the theatre in the Trendelenburg position for some hours and gave intravenous saline. The patient picked up wonderfully, but only passed 9 oz. of urine in the first twenty-four hours, though the amount of albumin had considerably diminished. In the next fourteen hours she passed 20 oz. of urine, and after this a normal quantity each day, albumin not being present after the fourth day. Three days after the operation diarrhœa commenced, consisting of very offensive watery material containing undigested milk. This diarrhœa continued in spite of treatment until death took place from exhaustion three days later, that is six days after the operation. During the whole of this time the patient was bright, had no headache, or visual disturbances, passed a normal quantity of urine, with a gradually diminishing amount of albumin which completely disappeared after the third day. The temperature was intermittent to 100 F., and once to 101.4 F., and the pulse varied from 100 to 140. There was never any rigidity of the abdomen. At the post-mortem examination there was a small amount of clear fluid in the peritoneal cavity. The intestines were much injected and contained very foul, thin, watery yellow material. The right ureter was caught in a ligature and was distended as was also the hylum of the kidney. Both kidneys were apparently healthy, both on macroscopic and microscopic examination. The abdominal and pelvic wounds were quite healthy. The lungs were very œdematous, but there was no consolidation. The heart was normal.

Specimen. The uterus is enlarged and has been completely removed by panhysterectomy. It is of a deep red, almost black, colour all over except for a V-shaped area on the anterior and posterior walls. This discoloration, and that of the broad ligaments which have shrunk very much in the preservative solution, is due to extravasated blood. On the posterior surfaces are several cracks not extending much deeper than through the peritoneal coat. The section through the tissues shows several

patches of extravasated blood; these are chiefly in the superficial layers under the peritoneal coat. There is a considerable increase of fibrous tissue but very little increase in the amount of elastic tissue.

Case II. M.E.B., aged 41, was admitted to St. Mary's Hospital on February 3, 1915, for severe hæmorrhage. She was seven months pregnant with her seventh child, and there was a considerable amount of albuminuria. The hæmorrhage commenced suddenly at 7.10 a.m., but she was not sent to the hospital until almost midnight. She was then very collapsed, with a pulse of 144 and temperature of 96 F., and the uterus was the size of full-time pregnancy and very tender. She was immediately taken to the theatre and Cæsarean section with hysterectomy performed. There was about half a pint of free blood in the abdominal cavity and a very large hæmatoma in the left broad ligament. The right broad ligament contained no blood. The uterus was filled with clotted blood, amongst which was the completely detached placenta and a dead child. She made a perfectly good recovery.

Case III. M.E.H., aged 38, eight and a half months pregnant with her eleventh child, was admitted to St. Mary's Hospital on August 28, 1915. There was a considerable amount of albuminuria. This patient was seized with sudden severe abdominal pain at 2 a.m. whilst in bed. She sent for the midwife, but though in a collapsed condition she was not sent to St. Mary's Hospital until ten hours later. On admission, the patient was very blanched and collapsed, with sighing respiration, and a thin uncountable pulse. The uterus was distended, very tender, and there was no sign of external bleeding. She was immediately taken to the theatre and Cæsarean hysterectomy performed, while at the same time intravenous injection of saline was given. The operation only occupied fifteen minutes, but the patient died fifteen minutes later. The uterus was distended with blood and the placenta was completely detached. Both broad ligaments were enormously distended with large hæmatoma, but there was no free blood in the peritoneal cavity. This patient was moribund on admission, but it was decided to perform the operation and give her the only chance, though a slight one, of recovery.

Case IV. S.N., aged 32, eight months pregnant with her ninth child, was admitted to St. Mary's Hospital on September 15, 1915. There was a large amount of albumin in the urine. Severe hæmorrhage commenced suddenly while she was in bed early in the morning, and she felt faint. The hæmorrhage slackened a little, but continued all day, and she was sent to the hospital at 4.30 p.m. On admission, she was very pale, pulse 140. The uterus was the size of full-time pregnancy, hard and very tender. The cervix admitted two fingers, but the external hæmorrhage was not severe and no placenta could be felt. Cæsarean hysterectomy was performed. The uterus was full of clotted blood; the placenta was entirely detached, and the child was dead. The woman was so anæmic that there was no bleeding from the uterine incision. There was no free blood in the abdominal cavity, but there was a very large hæmatoma in the left broad ligament and a smaller one in the right. It was only with the greatest difficulty that the bleeding could be controlled on the left side, as the vessels were lost in the blood clot, and the tissue as high as the third lumbar vertebræ had to be ligatured in the hope of catching all the vessels. The operation was done as rapidly as possible, but the patient's pulse could not be felt at the end of the operation. She was kept on the operating

table in front of a large fire, intravenous infusion of saline given, and also pituitary extract. She gradually recovered, and eventually made a perfectly good recovry.

Case V. H.H., aged 41, seven months pregnant with her ninth child, was admitted to St. Mary's Hospital on September 15, 1915. There was a large amount of albuminuria. Hæmorrhage commenced suddenly at 4 p.m. with severe abdominal pain, and she was admitted to the hospital three hours later. There was then free external hæmorrhage; the cervix admitted one finger; the uterus was hard, large and tender; the patient was collapsed and the pulse uncountable. Cæsarean hysterectomy was performed soon after admission. The uterus was filled with masses of blood-clot; the placenta completely detached, and the child was dead. There was a large hæmatoma in the right broad ligament, but none in the left though the hæmatoma on the right side did not extend over the pelvic brim as occurred in some of the other cases; there was much difficulty in controlling the oozing of the thin watery blood, but the operation on the whole was much easier than some of the previous ones. This patient made an uninterrupted recovery.

Case VI. M.R., aged 39, eight months pregnant with her thirteenth child, was admitted to St. Mary's Hospital on September 23, 1915. There was much albuminuria. Severe external hæmorrhage commenced in the afternoon, and a district nurse who saw her sent her to the hospital at once. On admission her general condition was fairly good, pulse 126, and temperature 98.2 F. The Resident Obstetrical Surgeon ruptured the membrane, applied a tight binder, and gave pituitary extract, but no contractions of the uterus occurred, and the hæmorrhage continued. Later in the evening I was sent for and did Cæsarean hysterectomy. There was no free blood in the peritonal cavity, and no hæmatoma of the broad ligaments. The uterus was full of blood-clots and the placenta was completely detached. The uterus made no attempt to contract after extraction of the child. This operation was performed much more methodically than any of the previous ones as the patient was in a much better general condition, and two ligatures were placed round each uterine and ovarian artery. At the end of the operation she was in a fairly good condition with a pulse of 120. Six hours later she was restless and cold, with sighing respiration, but her pulse was only 110, so we looked upon her condition as one of shock, but very soon afterwards she died. Post-mortem examination showed that the ligatures round the right uterine artery had slipped and the patient had bled to death, though we had been misled as to her condition by the pulse-rate not increasing.

Case VII. Mrs. A. J., 38 years of age, was admitted to St. Mary's Hospital on August 23rd, 1916. She was almost full-time with her ninth pregnancy. She had been bleeding all day and was sent in by a doctor with a diagnosis of placenta prævia. She was admitted at 3.15p.m. The cervix then admitted two fingers and the placenta could be felt rather high up on the right hand side. The hæmorrhage had then almost ceased. We gave her a quarter grain of morphia and kept her quiet in the hope that the cervix would dilate further before any operative interference was necessary, and that her general condition, which at that time was extremely bad, would improve.

At 8 p.m. the hæmorrhage recommenced; the cervix was then about one-third dilated and was fairly soft. As the hæmorrhage was very severe,

and the placenta could be felt, podalic version was considered the best treatment; this was quickly carried out by internal version and the patient left with a nurse holding on the child's leg.

Half an hour later I was again called to the patient; the bleeding had not ceased since the version was performed and she was then in a very collapsed condition. I then realised that though the placenta could be felt I was really dealing with a case of accidental hæmorrhage, as I have never seen a case of placenta prævia which continued to bleed after version had been performed. Moreover the patient had a large amount of albuminuria which is of very frequent occurrence with cases of accidental hæmorrhage and is very rare in cases of placenta prævia. The patient, however, was in too collapsed a condition to allow of abdominal section. I extracted the child and gave a hot intrauterine douche and three doses of pituitrin, but still the hæmorrhage continued, so I decided to do a vaginal hysterectomy. This was very rapidly performed by clamping the broad ligaments with large Spencer Wells which were left on and no time wasted in tying ligatures. Unfortunately the patient only lived for about one hour after the operation, though we tried every means of combatting the shock and hæmorrhage.

The operation performed in five of the cases was Cæsarean section through a longitudinal median abdominal and uterine incision. After extraction of the child the round and infundibulo-pelvic ligaments on both sides were seized with pressure forceps and cut, the utero-vesical peritoneum incised, the uterine arteries on both sides seized and cut and then the cervix across about the level of the internal os. After suturing the cervix and ligaturing the uterine arteries and the round and infundibulo-pelvic ligament, the cut edges of the peritoneum were drawn over the raw surface of the cervix and broad ligaments and the abdominal wound closed in three layers. This is one of the operations in which time is an essential factor, every minute saved, in some of the cases, being of the greatest importance: one of the operations was completed in fifteen minutes, though needless to say no time was lost in peritonizing the pelvic wound or in stitching up the abdomen in layers.

The remaining two cases were operated upon after delivery of the child per *vias naturales*, on account of persistent hæmorrhage from a flabby uterus which no treatment could stimulate into contraction. In Case I the abdomen was opened and panhysterectomy performed, in Case VII vaginal hysterectomy was rapidly performed with clamps instead of ligatures, as the patient's condition was too severe to allow of removal to the theatre and the performance of an abdominal operation.

All these seven cases were of the severest type of accidental hæmorrhage and all would undoubtedly have died if they had not been operated upon. They were all suffering very severely from the effects of the hæmorrhage, and in none of the cases did the

uterus show the slightest sign of contraction after removal of the child, so there was no option but to follow the Cæsarean section by hysterectomy. The final result was four deaths and three recoveries; of the five cases in which I performed Cæsarean hysterectomy two died and three recovered; but one of the deaths was due to the accident of a slipped ligature, which has only once previously occurred to me, and this case I believe would have been saved if I had opened the abdomen again. I thought, however, she was suffering from shock as her pulse-rate did not increase; at the end of the operation this patient was in a much better general condition than any of the others.

With regard to the other three deaths, one patient, No. III, was practically moribund at the time of admission, and I only did the operation in the very faint hope that she might be saved; she survived the operation only a quarter of an hour. This patient was sent to the hospital ten hours after the onset of symptoms, and her life would almost certainly have been saved if the midwife had realised the gravity of her condition earlier. One of the other deaths, No. I, took place six days after the operation with the symptoms of toxæmia, and the last, No. VII, was moribund when the operation was performed. A mortality of 57 per cent. is extremely high, but the patients representing the 43 per cent. would undoubtedly have died if the operation had not been performed, and the mortality is very considerably reduced if the two cases are eliminated which were practically moribund when the operation was performed. As was to be expected all the children were dead, the placentæ being completely detached.

The outstanding feature of these cases was the condition of the uterus; all, but one, containing a large hæmatoma in one or both broad ligaments, in some cases extending far above the pelvic brim and, in two of the cases, the condition had extended so far that the peritoneum had cracked and free blood had been poured into the peritoneal cavity. In the first and seventh cases, the patients operated upon for hæmorrhage after the birth of the child, the uterus had been douched and massaged frequently and it is possible the lacerations on the surface of one and the hæmatomata in the broad ligaments of both, may have been caused by trauma, though they had not been treated more vigorously than many uteri which have symptoms of post-partum hæmorrhage. Of the remaining five cases, four had a large hæmatoma in the broad ligament and one of these also had free blood in the peritoneal cavity: no treatment had been attempted in the case of these patients before the abdomen was opened, so the hæmorrhage must have been due to some local condition of the uterus or some general condition of the patient.

None of the seven cases I now record had the slightest chance of surviving had not the operation been performed, as not one of the uteri made the slightest effort to contract, except the first, and that maintained a persistent trickle of blood which almost killed the patient. But the condition found at the operation, hæmatoma of the broad ligament and free blood in the peritoneal cavity, quite unsuspected previously, should induce us to consider whether some of the less severe cases would not be better treated by Cæsarean section followed by hysterectomy if necessary, than the more conservative method. In all probability the two cases operated upon after the birth of the child, No. I and No. VII, would have been saved if Cæsarean section and hysterectomy had been performed earlier.

Pathology. All these uteri show an increased amount of elastic and fibrous tissue especially around the blood-vessels, but not more than is usually found in multiparous uteri, and apart from this I can find no change except extravasated blood in the uterine wall, more marked in the superficial layers especially under the peritoneal covering. Couvelaire considers this a constant feature in accidental hæmorrhage, but we must look upon it as the result of the condition, not the cause. In these cases the condition had gone much further, not only was the blood extravasated into the uterine wall but it had extended into the broad ligaments to form large hæmatomata, and in two cases had broken through the peritoneal covering of the uterus and had trickled into the peritoneal cavity.

Another constant feature was the presence of albuminuria. This occurs in the great majority of cases of accidental hæmorrhage, and I find it exceptional to meet with a case, slight or severe, in which this condition is not present.

The older teaching was that accidental hæmorrhage was caused by an accident, and I well remember, as a student, being warned not to allow pregnant women to do any work which necessitated the arms being raised above the head, such as the lifting of plates from a shelf, etc. It is very exceptional to see a case even remotely connected with an accident, and a large proportion commence to bleed during the night while in bed.

We must look much deeper to find the cause of this condition. In my opinion it will be found in some general condition of the patient, probably a toxæmia. My chief reason for this belief is founded on the large number of patients with accidental hæmorrhage who have albuminuria which entirely disappears a few days after confinement, not persisting as it does in cases of chronic nephritis.

This, of course, opens up a wide field for research, but when the toxin or toxins are found which produce eclampsia, acute yellow

atrophy of the liver, hyperæmesia gravidarum and chorea gravidum, it is more than likely we shall find them present in cases of accidental hæmorrhage.

I must emphasize the fact that I advocate Cæsarean hysterectomy only for those severe cases of accidental hæmorrhage which will not respond to the usual methods of treatment. Fortunately the great majority of cases of accidental hæmorrhage cease to bleed if the membranes are ruptured and ergot or pituitrin given and a tight binder applied, or if the vagina is tightly plugged, but if the hæmorrhage continues at all severely after one of these methods has been tried, Cæsarean hysterectomy should be performed before the patient's general condition is so severe that she will not stand an abdominal operation. Cases No. I and VII emphasize this point, and I believe they both would have been saved if I had operated before the birth of the child. Between Cases VI and VII almost a year elapsed in which I saw a number of cases of accidental hæmorrhage all of which responded to the usual methods of treatment: in none of these cases would I suggest Cæsarean hysterectomy, but the few cases which will not respond to ordinary methods can be saved by an abdominal operation if too much time has not been lost. It is for these cases I advocate Cæsarean hysterectomy.

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Case of Acute Strangulation of the Uterus by Torsion of the Body on the Cervix: Supra-cervical Hysterectomy: Recovery.

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ROTATION of the whole uterus with an ovarian or uterine tumour is not very uncommon, the displacement being at most something over half a revolution. I have never seen complete arrest of the blood supply from this cause, and I have not before seen a case like the following:—

On November 3, 1915, a rather frail lady, æt. 70, married, but never pregnant, complained after dinner of pelvic pain. Next morning she was better and took her breakfast in bed as usual; but she could not get up afterwards because the pain became intense and was accompanied by vomiting. Towards evening the temperature rose to 101°F. I saw her late that night with Dr. Hewetson and Dr. Watson, of Reigate, and found a hard, nearly round pelvic tumour, median in position and about four inches in diameter. Behind this, and also in the middle line, lay an elongated, irregularly-oval mass measuring apparently about $3\frac{1}{2}$ inches from above downwards, by $1\frac{1}{2}$ inches from side to side. This was fairly soft, but of uneven consistence. It seemed to be attached to the hard mass in front, and there was a small, soft, short cervix uteri below. The rectum was firmly compressed, but the abnormal parts, which were very tender, seemed to be slightly moveable as one mass in the pelvis. It was known that a fibromyoma existed before the patient's menstruation ceased, and it was easy to surmise that something had twisted, but the condition behind the hard tumour puzzled us all.

It was decided to open the abdomen at once, and on doing so a fibromyoma was exposed. When this was raised out of the pelvis by folding it backwards the condition shown diagramatically in Fig. 1 was discovered. There were no adhesions anywhere, but the fibromyoma and the body of the uterus were of a deep blue-black colour from congestion caused by a complete revolution of these parts on the cervix uteri. The left tube and ovary were above the site of the torsion, the right ovary was below, and the right tube was involved in it. Although the operation was performed only sixteen hours after the pain became severe and about twenty-eight hours from the first onset, the condition caused a distinctly un-

pleasant odour. The parts drawn in Fig. 2 were removed by dividing the uterus at the junction of the congested with the healthy tissues and securing the vessels which were few and small. The cut peritoneal edges were sewn together and when released the stump fell well down in the pelvis.

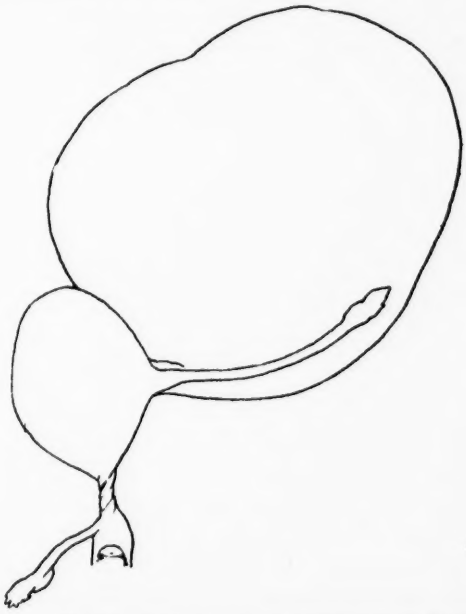


Fig 1.—Showing diagrammatically the relative proportions of the congested body and the senile cervix uteri, the tightness of the structure, and the portion of the ovaries.

This patient had always been slow in recovering from illness, and after the operation there was considerable difficulty and anxiety on account of an inactive state of the bowels accompanied by flatulent distension, but by a judicious use of intestinal stimulants recovery was gradually established. In the temporary absence of Dr. Hewetson, Dr. Watson guided the patient through the most critical stage, and he found pituitary extract definitely useful as a promoter of peristalsis in this case.

The uterine body, as shown in Fig. 2, was as big as that of a woman in the child-bearing period, but its size was due to an intense congestion. The cut surface, as drawn, has a wide area which does not suggest a constriction, but the parts were untwisted before they were divided and the removal was effected so as to take a wedge out of the part left, the result being a nearly flat surface.

There can be no doubt that before the torsion occurred the uterus was very soft from senility and stretched and narrowed above the vagina by traction of the tumour. It would hardly seem possible that the torsion found could exist without these conditions.

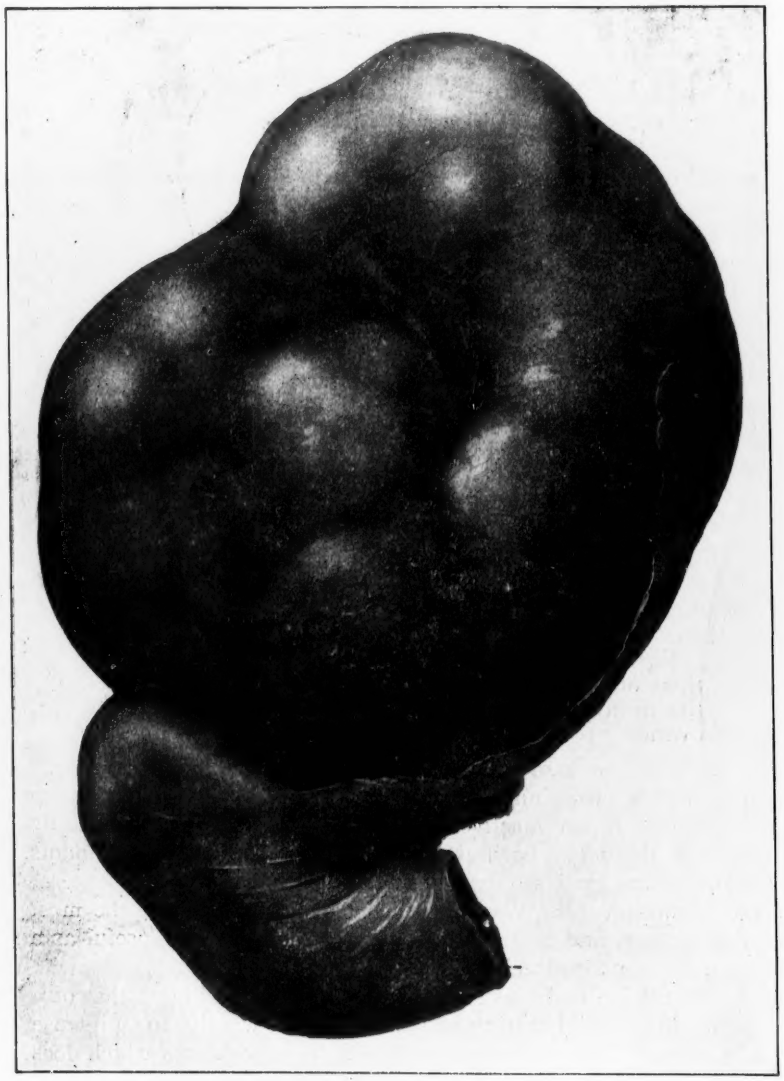


Fig. 2.—The uterus, tumour, and left ovary.

Fatal Case of Acute Hæmorrhagic Hepatitis following Toxæmia of Pregnancy.

By J. Bright Banister, M.A., M.D. (Cantab), F.R.C.S., (Edin.),

Physician, Queen Charlotte's Hospital; Surgeon to Out-Patients, Chelsea Hospital for Women; Gynæcologist, Prince of Wales' Hospital; and

R. Henry Stevens, M.R.C.S., L.R.C.P.,

Resident Medical Officer, Queen Charlotte's Hospital.

Mrs. F. The patient, in this case a ii-gravida, aged 34, was admitted under Mr. T. G. Stevens on August 25, at 10.30 in the evening. She had then been having pains for about two hours. The os was the size of half-a-crown, and she was in a very excitable and restless condition, with a feeble pulse of about 100, and temperature a little over normal.

She had a history of gastro-intestinal disturbance for the previous fortnight, with some vomiting and almost continuous pain in the upper part of the abdomen, together with slight diarrhœa, anorexia, and swelling of the legs. The symptoms, however, which seems to have struck her husband most forcibly during this period were the intense restlessness and mental distress, which she also manifested on admission.

She thought she had been passing less urine than usual, and complained of great thirst together with headache in the frontal region and epigastric pain.

There was considerable œdema of the lower extremities, and her complexion was very sallow, though not icteric.

The imminent onset of eclampsia was anticipated, in view of the fact that the urine (catheter specimen) gave a very heavy cloud of albumen on boiling. The patient was therefore freely purged and given a hot pack. As the pains were getting stronger her restlessness became so great that hyoscine gr. 1/100 and morphine gr. $\frac{1}{4}$ were administered subcutaneously, and at the end of the second stage, which occurred about five hours after admission, a few whiffs of chloroform were given.

On the following morning one of us (R.H.S.) was called to see the patient about 9.30, because she was jaundiced and had acute

epigastric pain. The temperature and pulse were both about 100, she was obviously suffering great pain, and she had great hyperæsthesia in the umbilical region and all down the right side; there was also severe referred pain in the *left* shoulder and hæmatemesis, these last two features being unlike a case of gallstones. The patient was markedly jaundiced and very restless. The abdomen was rigid and gave a tympanitic note to percussion. No tumour could be felt, but the liver dulness seemed reduced. A catheter drew off about two ounces of port-wine-coloured urine, which was the only specimen obtained after delivery. The vomiting, which was incessant, was of the "coffee-ground" type, with streaks of bright blood. It did not smell of phosphorus and was not luminous in the dark. The urine contained many blood-cells and much blood-pigment. It was loaded with albumen and gave a faint bile reaction. The most interesting thing about the urine was that it contained scattered leucin-cones, though no tyrosin-tufts were discovered. An urea estimation was unfortunately omitted, but it would not have been of great value as it would have been impossible to collect the urine for 24 hours owing to the fact that the patient had incontinence.

All these symptoms and signs, including the reduced area of liver dulness, were sufficient to justify a diagnosis of acute yellow atrophy, but here it is only fair to say that post mortem the liver was found in no way reduced in size, but merely compressed by the marked degree of meteorism present. Mr. T. G. Stevens, of St. Mary's, and Sir Wilmot Herringham, of St. Bartholomew's, both saw the patient, and concurred in the diagnosis.

The patient's condition became rapidly worse, although the temperature came down. The vomiting continued, though hæmatemesis ceased. There was a continuous trickle of hæmorrhage from the uterus, although it felt firm and well retracted. This metrorrhagia was uncontrollable by ergotin or hot douches. Morphia was administered on three or four occasions for the pain and restlessness. The patient complained of great hunger and thirst, but immediately vomited fluids taken by the mouth. Saline solution was given by the rectum and retained.

On the night of the 27th–28th the patient became delirious and passed fæces under her. These apparently contained altered blood. On the 28th she was, if possible, more restless, continually trying to rise and sinking back exhausted after each attempt. The temperature was rather subnormal and the jaundice had deepened.

In the evening she passed from delirium into coma, and died about forty hours after delivery.

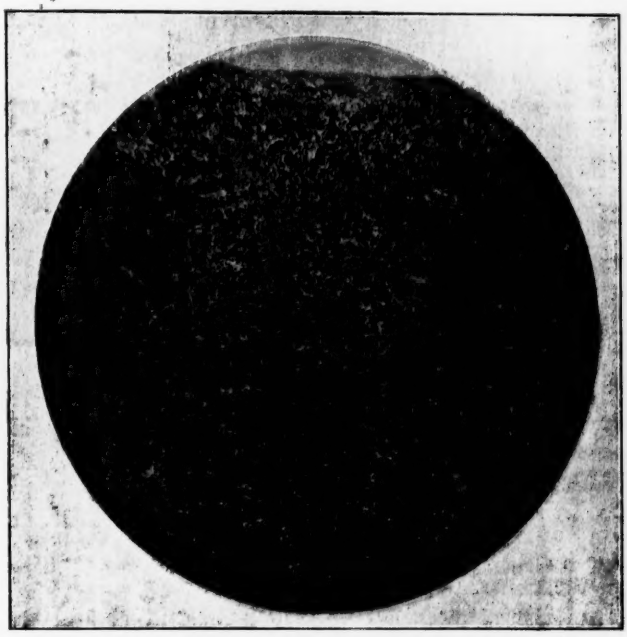
A post mortem examination of this case was performed within

six hours of death. The body was somewhat emaciated and deeply jaundiced. There was marked abdominal distension.

The brain was somewhat œdematous, but was otherwise perfectly normal. The pericardium contained about half an ounce of straw-coloured fluid. The heart was of normal size; its valves showed no signs of disease, but the musculature was softened throughout.

The lungs were markedly congested at the bases, but were crepitant throughout. The pleural cavity was normal.

The stomach and intestines were distended throughout, the former being half full of a dark " coffee-ground " fluid.



Liver from a case of very *acute hepatic toxæmia of pregnancy*. Patient died in thirty-six hours, deeply jaundiced, after continuous vomiting of " coffee-ground " material and a very violent delirium. The extravasation of blood throughout the section suggesting an acute toxæmia rapidly destroying the vessel walls and leading to widespread extravasation, *before* cellular necrotic changes had time to take place.

The spleen was soft and slightly enlarged, but the kidneys appeared comparatively normal. Microscopically, they showed a moderate amount of cloudy swelling, but no fat. The ureters and

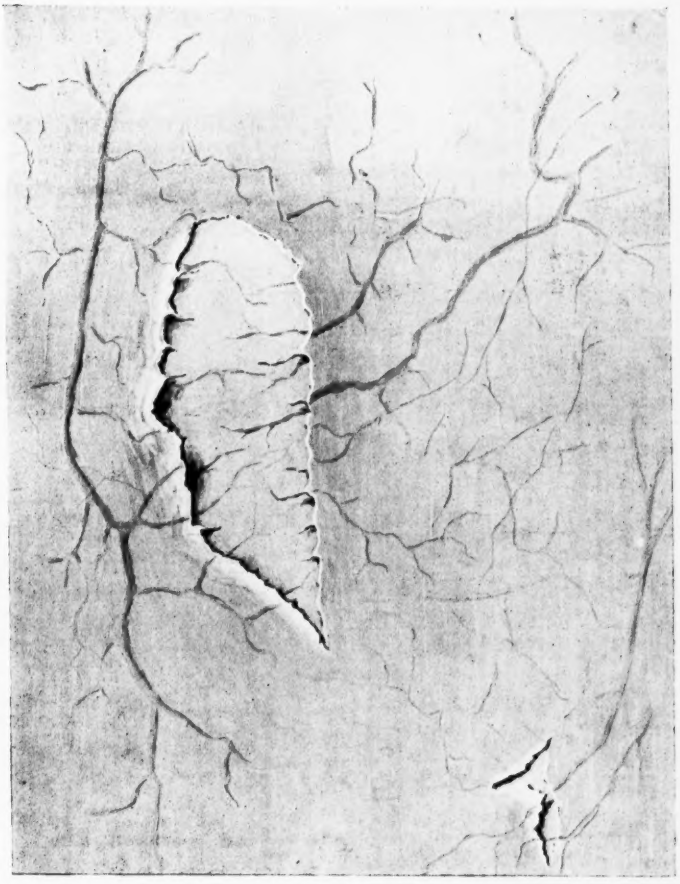
bladder were normal, the latter containing an ounce or so of very dark-coloured urine.

The liver weighed 56 ounces and was somewhat light in colour. Scattered over its surface hæmorrhagic areas could be seen beneath the capsule which was not thickened. These hæmorrhagic areas were found on section to be scattered broadcast throughout the organ. Microscopic section showed the liver substance broken up by multiple areas of hæmorrhage, the liver cells being entirely destroyed in places, while in other places they were not markedly changed (see plate).

The pathological findings suggest the adoption of the title acute hæmorrhagic hepatitis, for the size and colour of the liver do not correspond with the findings in cases of so-called acute yellow atrophy. To us the case suggests a very acute toxæmia, the action of which was primarily upon the walls of the liver capillaries causing rupture and a consequent flooding of the adjacent liver substance with blood.

Partial Rupture of an Ovarian Cyst weighing 32 pounds with Great Loss of Blood in a Girl 15 years of age.

By Palmer Findley, M.D., F.A.C.S.,
Professor of Gynæcology, College of Medicine, University of Nebraska.



Rupture of inner lining of cyst involving branches of blood vessels. Escape of large quantity of blood within cyst. Weight of cyst 32 pounds.

Miss B., age 15, a girl of unusual intelligence, thought herself perfectly well until two weeks before admission to the hospital when she began to complain of persistent headache and backache,

together with general lassitude. A few days later the attention of her mother was called to the enlargement of the abdomen. On examination the abdomen was found to be enormously distended with fluid; breathing was interfered with and the heart's action was embarrassed. She was very anæmic (hæmoglobin 40%).

On February 4 1916, the abdomen was tapped and about six litres of bloody fluid withdrawn. Forty-eight hours later an incision, extending from the pubis to near the ensiform cartilage, was made, and a cyst of the right ovary removed intact which weighed, together with the fluid previously removed, thirty-two pounds. The cyst was thin-walled and multilocular. Within the cyst was about one litre of clotted blood and the remaining fluid was dark as grape juice. There was no twist of the pedicle and no evidence of malignancy.

Splitting the cyst open the origin of the escaped blood was found in a rent through the inner lining of the cyst which involved branches of arteries. The rent was probably the result of rapid distention of the cyst. With the escape of the blood within the cyst came rapid enlargement of the cyst, acute anæmia and general debility.